













# **PRACTICE OF MEDICINE**

**VOLUME IX**



# PRACTICE OF MEDICINE

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# CONTENTS

## VOLUME IX

### SECTION XIII: DISORDERS OF METABOLISM

CHAPTER	PAGE
I. GOUT . . . . .	1
By WILLIAM FLETCHER MCPHEDRAN	
Definition . . . . .	1
Etiology . . . . .	1
Predisposing Causes . . . . .	1
Symptomatology . . . . .	3
Clinical History . . . . .	3
Physical Findings . . . . .	5
Laboratory Findings . . . . .	7
Special Examinations . . . . .	10
Diagnosis . . . . .	11
Complications . . . . .	12
Clinical Varieties . . . . .	12
Aberrant Types of Gout . . . . .	12
Gouty Affections of the Skin . . . . .	13
Digestive System . . . . .	13
The Eye . . . . .	14
Nervous System . . . . .	14
Treatment . . . . .	14
Diet . . . . .	14
Climatology . . . . .	18
Hydrotherapy . . . . .	18
Medicinal Treatment . . . . .	19
Radium and X-ray Treatment of Gout . . . . .	20
Surgical Indications . . . . .	20
Management of Convalescence . . . . .	20
Prognosis . . . . .	21
Pathology . . . . .	21
Physiology: Uric Acid Metabolism . . . . .	25
Theories of Gout . . . . .	33
Historical Summary . . . . .	35
II. OBESITY . . . . .	39
By WILLIAM FLETCHER MCPHEDRAN	
Definition . . . . .	39
Etiology . . . . .	39
Predisposing Causes . . . . .	39
Symptomatology . . . . .	39
Physical Findings . . . . .	40
Special Examinations . . . . .	41
Fröhlich's Syndrome . . . . .	41



	PAGE
Diagnosis . . . . .	41
Dercum's Disease . . . . .	42
Complications . . . . .	42
Association with Other Diseases . . . . .	42
Treatment . . . . .	42
Prophylaxis . . . . .	42
General Management . . . . .	42
Diet . . . . .	43
Treatment of Symptoms . . . . .	47
Hydrotherapy: Mechanotherapy . . . . .	47
Organotherapy . . . . .	48
Exercise . . . . .	48
Medicinal Treatment . . . . .	49
Prognosis . . . . .	49
Pathology . . . . .	49
Fat Metabolism . . . . .	50
 III. LIPOMATOSIS . . . . .	 53
BY WILLIAM FLETCHER MCPHEDRAN	
Etiology . . . . .	53
Symptomatology . . . . .	53
Clinical History . . . . .	53
Mode of Onset . . . . .	53
Symptoms during Progress of Disease . . . . .	53
Physical Findings . . . . .	53
Diagnosis . . . . .	54
Clinical Varieties . . . . .	54
Treatment . . . . .	55
Pathology . . . . .	55
 IV. HEMOCHROMATOSIS . . . . .	 57
BY WILLIAM FLETCHER MCPHEDRAN	
Etiology . . . . .	57
Predisposing Causes . . . . .	57
Symptomatology . . . . .	59
Physical Findings . . . . .	59
Laboratory Findings . . . . .	59
Diagnosis . . . . .	60
Treatment . . . . .	60
Prognosis . . . . .	61
Pathology . . . . .	61
 V. OCHRONOSIS . . . . .	 65
BY WILLIAM FLETCHER MCPHEDRAN	
Etiology . . . . .	65
Symptomatology . . . . .	65
Laboratory Findings . . . . .	66
Diagnosis . . . . .	66
Treatment . . . . .	66
Pathology . . . . .	66

CHAPTER	PAGE
VI. DIABETES MELLITUS . . . . .	69

BY HERMAN O. MOSENTHAL

Definition . . . . .	69
Normal Carbohydrate Metabolism . . . . .	70
Origin of Glucose from Protein—D:N Ratio . . . . .	70
The Blood Sugar . . . . .	71
Tests for Blood Sugar . . . . .	71
The Normal and the Diabetic Blood Sugar . . . . .	71
Glycosuria . . . . .	74
Renal (Diabetes) Glycosuria; the Relation of the Kidney to the Blood Sugar . . . . .	74
Other Glycosurias; the Relation of the Endocrine Glands to Carbohydrate Metabolism . . . . .	78
The Diagnosis of Diabetes Mellitus . . . . .	78
The Identification of Glucose in the Urine . . . . .	79
Test for Carbohydrate Tolerance . . . . .	80
Acidosis . . . . .	81
The Chemistry of Acidosis . . . . .	81
Degree of Acidosis . . . . .	86
Symptoms of Acidosis . . . . .	90
Etiology . . . . .	91
Symptomatology . . . . .	94
Onset . . . . .	94
Findings in the Urine . . . . .	95
Glycosuria . . . . .	96
Results of Polyuria . . . . .	97
Appetite . . . . .	97
Loss of Weight and Emaciation . . . . .	97
Acidosis . . . . .	98
Carbohydrate Tolerance . . . . .	98
History Forms . . . . .	98
Complications . . . . .	98
Skin . . . . .	98
Heart and Blood-vessels . . . . .	99
Kidney . . . . .	99
Lungs . . . . .	100
Digestive System . . . . .	101
Nervous System . . . . .	101
Special Senses . . . . .	101
Clinical Types . . . . .	101
Treatment . . . . .	103
The Use of Insulin in Diabetes Mellitus . . . . .	125
Course and Prognosis . . . . .	133

VII. DIABETES INSIPIDUS . . . . .	135
-----------------------------------	-----

BY WILLIAM FLETCHER MCPHEDRAN

Definition . . . . .	135
Etiology . . . . .	135
Predisposing Causes . . . . .	135

CHAPTER	PAGE
Symptomatology . . . . .	138
Clinical History . . . . .	138
Physical Examination . . . . .	139
Laboratory Findings . . . . .	139
Diagnosis . . . . .	140
Complications and Association with Other Diseases . . . . .	140
Clinical Varieties . . . . .	140
Treatment . . . . .	140
Prophylaxis . . . . .	140
Medicinal Treatment . . . . .	141
Surgical Indications . . . . .	142
Prognosis . . . . .	142
Pathology . . . . .	142

## VIII. RICKETS . . . . . 145

BY FRANK C. NEFF

Definition . . . . .	145
Etiology . . . . .	145
Predisposing Causes . . . . .	145
Diet . . . . .	147
Experimental Studies . . . . .	148
Symptomatology . . . . .	149
Physical Findings . . . . .	149
Laboratory Findings . . . . .	152
X-ray Findings . . . . .	152
Diagnosis . . . . .	152
Sequelæ . . . . .	154
Association with Other Diseases . . . . .	154
Treatment . . . . .	155
Prophylaxis . . . . .	155
Diet . . . . .	156
Medicinal Treatment: General Management . . . . .	156
Prognosis . . . . .	157
Pathology . . . . .	157
Gross Changes . . . . .	157
Minute Changes . . . . .	158
Chemical Changes . . . . .	158
Historical Summary . . . . .	159
Sociological Aspects of Rickets . . . . .	159

## IX. SCURVY . . . . . 161

BY EDWARD B. VEDDER

Definition . . . . .	161
History . . . . .	161
Etiology: Development of Knowledge . . . . .	163
Symptomatology . . . . .	166
The Depletion Period . . . . .	166
Mode of Onset . . . . .	166
General Symptoms . . . . .	166
Special Symptoms . . . . .	169
Diagnosis . . . . .	170
Association with Other Diseases . . . . .	170
Pathology . . . . .	171

# CONTENTS

ix

	PAGE
Gross Pathology . . . . .	171
Microscopic Anatomy . . . . .	172
Treatment . . . . .	172
Prophylaxis . . . . .	172
Medicinal Treatment . . . . .	174
General Management . . . . .	175
Prognosis . . . . .	176

## X. INFANTILE SCURVY . . . . . 179

BY FRANK C. NEFF

Definition . . . . .	179
Etiology . . . . .	179
Predisposing Causes . . . . .	179
Experimental Studies . . . . .	180
Symptomatology . . . . .	182
Physical Findings . . . . .	182
Constitutional Symptoms . . . . .	183
Laboratory Findings . . . . .	183
Roentgen-ray Findings . . . . .	184
Diagnosis . . . . .	185
Association with Other Diseases . . . . .	185
Treatment . . . . .	186
Prognosis . . . . .	186
Pathology . . . . .	186
Historical Summary . . . . .	187
Sociological Aspects . . . . .	187

## XI. BERIBERI . . . . . 189

BY EDWARD B. VEDDER

Definition . . . . .	189
Etiology . . . . .	189
Epidemiological . . . . .	190
The Human Feeding Experiments of Fraser and Stanton . . . . .	191
Animal Experiments . . . . .	191
Symptomatology . . . . .	193
The Depletion Period . . . . .	193
Types of the Disease . . . . .	194
Infantile Beriberi . . . . .	194
The Onset and Course . . . . .	194
Symptoms Produced by Degeneration of the Nervous System . . . . .	196
Edema and Serous Effusions . . . . .	197
The Circulatory Symptoms . . . . .	197
Gastro-intestinal Disturbances . . . . .	198
Urinary Findings . . . . .	198
Aphonia . . . . .	199
Differential Diagnosis . . . . .	199
Complications . . . . .	200
Pathology . . . . .	200
Treatment . . . . .	201
Prophylaxis . . . . .	201
Medicinal Treatment . . . . .	202
Dietetic Treatment . . . . .	202
Prognosis . . . . .	203

XII. PELLAGRA . . . . .	205
-------------------------	-----

By JOSEPH GOLDBERGER

Synonyms . . . . .	205
Etiology . . . . .	205
Infectious versus Dietary Origin . . . . .	206
Predisposing Causes . . . . .	210
Symptomatology . . . . .	212
Clinical History . . . . .	212
Mode of Onset . . . . .	212
Course . . . . .	213
Individual Symptoms during Course of Disease . . . . .	214
Pseudo-pellagra . . . . .	223
Diagnosis . . . . .	223
Complications . . . . .	225
Sequelæ . . . . .	225
Association with Other Diseases . . . . .	225
Clinical Types . . . . .	226
Treatment . . . . .	226
Preventive . . . . .	226
Curative . . . . .	227
Local Treatment . . . . .	228
Climatology . . . . .	228
Medicinal Treatment . . . . .	229
Prognosis . . . . .	230
Pathology . . . . .	231
History . . . . .	231
Distribution . . . . .	233

## SECTION XIV: DISEASES OF THE NERVOUS SYSTEM

INTRODUCTION . . . . .	235
------------------------	-----

By JULIUS GRINKER

I. INJURIES AND DISEASES OF THE PERIPHERAL NERVES . . . . .	237
---	-----

By CHARLES METCALFE BYRNES

Injuries of the Peripheral Nerves . . . . .	237
Anatomy . . . . .	237
The Processes of Degeneration . . . . .	238
The Process of Regeneration . . . . .	240
Etiology . . . . .	242
Nerve Lesions Resulting from Injury . . . . .	242
Symptomatology . . . . .	244
Symptoms of Nerve Injury . . . . .	244
History of Injury . . . . .	245
General Examination . . . . .	246
Clinical Features of Complete Nerve Lesions . . . . .	248
Motor Symptoms . . . . .	248
Sensory Symptoms . . . . .	252

# CONTENTS

xi

CHAPTER	PAGE
Trophic and Vasomotor Symptoms . . . . .	254
Clinical Features of Incomplete Nerve Lesions . . . . .	255
Causalgia . . . . .	255
Treatment of Causalgia . . . . .	257
Clinical Evidences of Nerve Regeneration . . . . .	259
Treatment . . . . .	261
General Treatment of Nerve Injuries . . . . .	261
Indications and Contra-indications for Surgical Intervention . . . . .	261
Choice of Operative Method . . . . .	262
Postoperative Treatment . . . . .	265
Prognosis . . . . .	265
Diseases of the Peripheral Nerves . . . . .	267
Neuritis . . . . .	267
Definition . . . . .	267
Etiology . . . . .	268
Symptomatology . . . . .	269
Diagnosis . . . . .	271
Treatment . . . . .	272
Prognosis . . . . .	274
Pathology . . . . .	274
Neuralgia . . . . .	275
Tumor of Nerves . . . . .	276
Herpes Zoster . . . . .	278
Definition . . . . .	278
Etiology . . . . .	278
Symptomatology . . . . .	280
Treatment . . . . .	281
Prognosis . . . . .	281
Pathology . . . . .	281
Bibliography . . . . .	283

## II. DISEASES OF THE SPINAL CORD . . . . . 289

By EDWARD LIVINGSTON HUNT

Progressive Muscular Atrophy . . . . .	289
Etiology . . . . .	289
Symptomatology . . . . .	289
Diagnosis . . . . .	292
Treatment . . . . .	292
Prognosis . . . . .	292
Pathology . . . . .	293
Myelitis . . . . .	293
Acute Myelitis . . . . .	293
Compression Myelitis . . . . .	299
Chronic Myelitis . . . . .	303
Amyotrophic Lateral Sclerosis . . . . .	304
Etiology . . . . .	304
Symptomatology . . . . .	305
Diagnosis . . . . .	307
Complications . . . . .	308
Clinical Types . . . . .	308
Treatment . . . . .	308
Pathology . . . . .	309

CHAPTER	PAGE
Historical Summary . . . . .	309
Spinal Meningitis . . . . .	310
External Pachymeningitis . . . . .	310
Internal Pachymeningitis . . . . .	311
Acute Spinal Leptomeningitis . . . . .	312
Chronic Spinal Leptomeningitis . . . . .	316
Multiple Sclerosis . . . . .	317
Etiology . . . . .	317
Symptomatology . . . . .	317
Diagnosis . . . . .	320
Complications . . . . .	320
Sequelæ . . . . .	321
Association with Other Diseases . . . . .	321
Clinical Varieties . . . . .	321
Treatment . . . . .	321
Prognosis . . . . .	321
Pathology . . . . .	322
Historical Summary . . . . .	322
Subacute Cord Degeneration . . . . .	322
Etiology . . . . .	322
Symptomatology . . . . .	322
Diagnosis . . . . .	323
Complications and Sequelæ . . . . .	323
Treatment . . . . .	323
Prognosis . . . . .	324
Pathology . . . . .	324
Historical Summary . . . . .	324
Syringomyelia . . . . .	324
Definition . . . . .	324
Etiology . . . . .	324
Symptomatology . . . . .	325
Diagnosis . . . . .	328
Complications . . . . .	328
Association with Other Diseases . . . . .	328
Clinical Varieties . . . . .	328
Treatment . . . . .	329
Prognosis . . . . .	330
Pathology . . . . .	330
Historical Summary . . . . .	331
Muscular Dystrophies . . . . .	331
Etiology . . . . .	332
Symptomatology . . . . .	332
Clinical Varieties . . . . .	334
Treatment . . . . .	335
Prognosis . . . . .	335
Pathology . . . . .	335
Historical Summary . . . . .	336
III. TUMORS OF THE SPINAL CORD . . . . .	377
BY ISRAEL STRAUSS	
Definition . . . . .	377
Etiology . . . . .	377

# CONTENTS

xiii

CHAPTER	PAGE
Predisposing Causes . . . . .	377
Symptomatology . . . . .	338
Extramedullary Tumors . . . . .	338
Intramedullary Growths . . . . .	348
Localization . . . . .	349
Tumors in the Cervical Region of the Cord . . . . .	350
Tumors of the Thoracic Cord . . . . .	360
Tumors of the Lumbar and Sacral Cord . . . . .	361
Tumors of the Conus Medullaris . . . . .	365
Diagnosis . . . . .	366
Differential Diagnosis . . . . .	366
Diagnosis on Laboratory Findings . . . . .	379
Treatment . . . . .	380
Course, Duration and Prognosis . . . . .	383
Pathology . . . . .	387
Extramedullary Tumors . . . . .	387
Intramedullary Tumors . . . . .	390

## IV. DIAGNOSIS AND LOCALIZATION OF BRAIN DISEASES 395

By ALFRED GORDON

Cerebral Localizations . . . . .	396
Introduction . . . . .	396
Frontal Lobe . . . . .	397
Prefrontal Region . . . . .	397
Frontal Lobe Proper . . . . .	399
The Upper Two Convolutions . . . . .	399
Third Frontal Convolution . . . . .	401
Aphasia . . . . .	401
Motor Aphasia . . . . .	402
Sensory Aphasia . . . . .	403
Transcortical Aphasia . . . . .	404
Amnesic Aphasia or Verbal Amnesia . . . . .	405
Optic Aphasia . . . . .	405
Paraphasia . . . . .	405
Total Aphasia . . . . .	407
Agraphia . . . . .	407
Aphasia in Right- and Left-handed Individuals . . . . .	409
Anarthria . . . . .	410
Aphasia According to the Views of Pierre Marie . . . . .	412
Pre-rolandic Area . . . . .	414
Jacksonian or Focal Epilepsy . . . . .	417
Post-rolandic Area . . . . .	421
Parietal Lobe Proper . . . . .	421
Disturbances of Stereognosis . . . . .	422
Sensory Disturbances of Cerebral Origin: Hemianesthesia . . . . .	423
Occipital Lobe: Hemianopsia . . . . .	424
Temporosphenoidal Lobe . . . . .	430
Mesial Surface of the Hemisphere . . . . .	431
Hippocampal Region . . . . .	431
Basal Ganglia . . . . .	433
Thalamus Opticus . . . . .	434
Corpora Striata . . . . .	435



CHAPTER	PAGE
The Red Nucleus . . . . .	439
Corpora Quadrigemina . . . . .	440
Internal Capsule . . . . .	441
Corpus Callosum . . . . .	443
Apraxia . . . . .	445
Cerebral Ventricles . . . . .	448
Third Ventricle . . . . .	448
Hydrocephalus . . . . .	449
Lateral Ventricles . . . . .	457
Pyocephalia . . . . .	458
Ventricular Hemorrhage . . . . .	460
Base of the Brain . . . . .	462
Extreme Anterior Portion . . . . .	463
Interpeduncular Region . . . . .	463
Hypophyseal Region . . . . .	463
The Pons . . . . .	467
Medulla Oblongata . . . . .	472
Acute Superior Polio-encephalitis . . . . .	473
Acute Inferior Polio-encephalitis . . . . .	474
Chronic Superior Polio-encephalitis . . . . .	477
Chronic Inferior Polio-encephalitis . . . . .	477
Pseudo-bulbar Palsy . . . . .	480
Asthenic Bulbar Paralysis . . . . .	482
Hemorrhage and Softening of the Medulla . . . . .	485
Compression of the Medulla . . . . .	485
Tumors of the Fourth Ventricle . . . . .	486
Localizing Diagnosis of Bulbar Symptoms . . . . .	487
Cerebellum . . . . .	488
Cerebellar Syndrome . . . . .	490
Cerebellar Hemiplegia . . . . .	494
Cerebellar Parasyndrome . . . . .	495
Cerebellar Tumors . . . . .	497
Abscess of the Cerebellum . . . . .	499
Cerebellar Heredo-ataxia . . . . .	503
Intracranial Hypertension and Tumors of the Brain . . . . .	505
Intracranial Hypertension . . . . .	523
Tumors of the Brain . . . . .	510
Treatment of Intracranial Hypertension and Tumors . . . . .	517
Tumors of the Pineal Body . . . . .	520
Inflammation of the Brain and Brain Shock . . . . .	524
Encephalitis . . . . .	524
Acute Non-suppurative Encephalitis . . . . .	525
Acute Suppurative Encephalitis . . . . .	528
Chronic Encephalitis . . . . .	533
Lethargic Encephalitis . . . . .	545
Concussion of the Brain . . . . .	546
Nervous Disorders Following Violent Explosions . . . . .	548
V. APOPLEXY . . . . .	555

BY ALFRED GORDON

Hemorrhage . . . . .	555
Pathology . . . . .	555

# CONTENTS

XV

CHAPTER	PAGE
Etiology . . . . .	557
Symptoms . . . . .	557
Softening of the Brain . . . . .	558
Pathology . . . . .	558
Etiology . . . . .	560
Symptoms . . . . .	560
Hemiplegia . . . . .	561
Symptoms . . . . .	561
Complications . . . . .	567
Prognosis of Apoplexy and Evolution of Hemiplegia . . . . .	570
Diagnosis of Apoplexy and Hemiplegia . . . . .	571
Diagnosis of Apoplexy . . . . .	571
Diagnosis of Hemiplegia . . . . .	574
Monoplegia . . . . .	576
Diagnosis and Localization . . . . .	576
Treatment of Apoplexy and Hemiplegia . . . . .	577
Syphilitic Hemiplegia . . . . .	580
Ingravescent or Progressive Apoplexy . . . . .	580
Delayed Apoplexy . . . . .	580
Homolateral Hemiplegia . . . . .	581
Intermittent Closing of Cerebral Arteries and Transitory Hemiplegia . . . . .	582
Cerebral Arteriosclerosis . . . . .	583
Meningeal Hemorrhage . . . . .	584
Cerebrosubarachnoid Variety . . . . .	584 •
Meningocerebral Form . . . . .	584
Meningo-encephalitis in Young Individuals . . . . .	584
Meningeal Hemorrhage . . . . .	586
Meningeal Hemorrhage Following Explosions, but Without External Injury . . . . .	587
Pachymeningitis Hemorrhagica Interna . . . . .	589
Meningeal Hemorrhage in the Newly Born . . . . .	590
Thrombosis of the Intracranial Sinuses . . . . .	593
Varieties . . . . .	593
Pathology . . . . .	593
Symptoms . . . . .	593
Course and Prognosis . . . . .	595
Diagnosis . . . . .	595
Treatment . . . . .	595
 VI. ENCEPHALITIS . . . . .	 597
By H. H. HOPPE	
Exudative Encephalitis . . . . .	597
Etiology . . . . .	597
Pathology . . . . .	597
Acute Hemorrhagic Cortical Encephalitis . . . . .	598
Etiology . . . . .	598
Pathological Anatomy . . . . .	599
Symptomatology . . . . .	602
Course, Duration and Termination . . . . .	604
Diagnosis . . . . .	604
Treatment . . . . .	606

CHAPTER	PAGE
Prognosis . . . . .	606
Polio-encephalitis Superior or Wernicke's Disease . . . . .	607
Etiology . . . . .	607
Pathology . . . . .	608
Symptomatology . . . . .	608
Diagnosis . . . . .	608
Prognosis . . . . .	608
Epidemic Lethargic Encephalitis . . . . .	608
Etiology . . . . .	609
Symptomatology . . . . .	609
Prognosis . . . . .	609
Tuberculous Localized Meningo-encephalitis . . . . .	609
Etiology . . . . .	609
Pathology . . . . .	610
Symptomatology . . . . .	610
Encephalitis of the New-born . . . . .	612
 VII. ABSCESS OF THE BRAIN . . . . .	 615
BY H. H. HOPPE	
Bergman's Classification of Abscess of the Brain . . . . .	615
Traumatic Abscesses . . . . .	615
Etiology . . . . .	616
Pathology . . . . .	617
Superficial Abscesses . . . . .	617
Deep Abscesses . . . . .	617
Symptomatology . . . . .	618
Superficial Abscesses . . . . .	618
Deep or Latent Abscesses . . . . .	619
Symptoms Due to Deep-seated Suppuration . . . . .	619
Symptoms Due to Increased Intracranial Pressure . . . . .	620
Focal Symptoms . . . . .	620
Course of Disease . . . . .	622
Diagnosis . . . . .	622
Superficial Abscesses . . . . .	622
Deep or Latent Abscesses . . . . .	622
Subdural Hemorrhage . . . . .	623
Traumatic Neurosis . . . . .	623
Serous Meningitis . . . . .	623
Otitic Sinus Thrombosis . . . . .	624
Treatment . . . . .	624
Superficial Abscesses . . . . .	624
Deep or Latent Abscesses . . . . .	624
Prognosis . . . . .	624
Superficial Abscesses . . . . .	624
Deep or Latent Abscesses . . . . .	624
Abscesses due to Purulent Inflammations of the Bone . . . . .	625
Tuberculous Abscesses . . . . .	627
Metastatic Abscesses . . . . .	627
So-called Idiopathic Abscesses . . . . .	628

# CONTENTS

xvii

CHAPTER	PAGE
VIII. BRAIN TUMORS . . . . .	631

By H. H. HOPPE

Introduction . . . . .	631
Etiology . . . . .	631
Specific Organism . . . . .	631
Trauma . . . . .	632
Sex . . . . .	632
Frequency . . . . .	632
Pathology . . . . .	633
Glioma . . . . .	633
Sarcoma . . . . .	636
Tubercles . . . . .	637
Gummata . . . . .	638
Fibromata . . . . .	640
Carcinomata . . . . .	640
Adenomata . . . . .	640
Cysts . . . . .	640
Angiomata . . . . .	640
Psammomata . . . . .	641
Lipomata . . . . .	641
Aneurysms . . . . .	641
Increased Intracranial Pressure . . . . .	641
Choked Disk . . . . .	642
Local Changes . . . . .	643
Symptomatology . . . . .	644
General Symptoms . . . . .	644
Localizing Signs . . . . .	650
Brain-tumor Symptom-complex with Termination in Recovery:	
Pseudo-brain Tumor . . . . .	686
Course and Duration . . . . .	693
Diagnosis . . . . .	693
Differential Diagnosis . . . . .	693
The X-ray as an Aid in Diagnosis . . . . .	697
Treatment . . . . .	698
Medical . . . . .	698
Surgical . . . . .	698
Prognosis . . . . .	705

IX. DISEASES OF SPECIAL NERVES . . . . .	709
--	-----

By CHARLES METCALFE BYRNES

The Cervical Nerves . . . . .	709
Cervico-occipital Neuralgia . . . . .	710
Indurative Headache . . . . .	710
Phrenic Nerve . . . . .	713
The Brachial Plexus . . . . .	714
Anatomy . . . . .	714
Diseases of the Brachial Nerves . . . . .	716
Paralysis of the Brachial Plexus . . . . .	716
Combined Palsies of the Upper Extremity . . . . .	717
Lesions of the Upper Trunk—the Duchenne-Erb or Upper Type of Palsy . . . . .	717

CHAPTER	PAGE
Lesions of the Lower Trunk—Klumpke or Lower Arm Type of	
Paralysis . . . . .	719
Obstetrical Paralysis—Duchenne-Erb Birth Palsy . . . . .	719
Cervical Rib . . . . .	721
Posterior Thoracic Nerve . . . . .	725
Suprascapular Nerve . . . . .	727
Axillary or Circumflex Nerve . . . . .	728
Radial or Musculospiral Nerve . . . . .	729
Median Nerve . . . . .	732
Musculocutaneous Nerve . . . . .	732
Ulnar Nerve . . . . .	734
The Intercostal Nerves . . . . .	737
The Lumbar and Sacral Plexuses . . . . .	737
Lumbar Plexus . . . . .	737
Sacral Plexus . . . . .	739
External Cutaneous Nerve . . . . .	739
Meralgia Paresthetica . . . . .	739
Obturator Nerve . . . . .	741
Femoral or Anterior Crural Nerve . . . . .	741
Neuritis of the Femoral Nerve . . . . .	742
Superior Gluteal Nerve . . . . .	742
Sciatic Nerve . . . . .	743
Tibial or Internal Popliteal Nerve . . . . .	744
Common Peroneal or External Popliteal Nerve . . . . .	745
Plantar Nerves . . . . .	746
The Sciaticas . . . . .	746
Definition . . . . .	746
Types of Ischialgia . . . . .	747
Incidence . . . . .	747
Etiology . . . . .	747
Symptomatology . . . . .	749
Special Methods of Examination . . . . .	750
Lasegue's Sign . . . . .	750
Kernig's Sign . . . . .	751
Patrick's Sign . . . . .	751
Sign of the Great Toe . . . . .	752
Sensory Achilles Sign . . . . .	752
Laboratory Examinations . . . . .	753
Diagnosis . . . . .	753
Complications . . . . .	754
Treatment . . . . .	754
Prognosis . . . . .	755
Pathology . . . . .	755
Multiple Neuritis . . . . .	755
Types of Multiple Neuritis . . . . .	756
Etiology . . . . .	757
Symptoms of Multiple Neuritis in General . . . . .	759
Sensory Symptoms . . . . .	760
Motor Symptoms . . . . .	761
Cranial Motor Nerves . . . . .	761
Sphincter Disorders . . . . .	762
Reflexes . . . . .	762

# CONTENTS

xix

CHAPTER	PAGE
Trophic and Vasomotor Symptoms . . . . .	762
Mental Disturbances . . . . .	763
Diagnosis . . . . .	763
Complications . . . . .	764
Treatment . . . . .	765
Prognosis . . . . .	766
Pathology . . . . .	766
Special Forms of Multiple Neuritis . . . . .	767
Alcoholic Neuritis . . . . .	767
Arsenical Neuritis . . . . .	768
Neuritis Due to Lead Poisoning . . . . .	769
Diabetic Neuritis . . . . .	769
Diphtheritic Paralysis . . . . .	770
Recurrent Polyneuritis . . . . .	771
Progressive Interstitial Hypertrophic Neuritis . . . . .	771
Acute Febrile Polyneuritis and Neuronitis . . . . .	772
Bibliography . . . . .	773



# LIST OF ILLUSTRATIONS

## SECTION XIII: DISORDERS OF METABOLISM

### CHAPTER I

#### GOUT

DIAGRAM	PAGE
1. Structure of the purin molecule and its derivatives . . . . .	26
2. Catabolism of nucleoproteins to uric acid and allantoin . . . . .	27

### CHAPTER VI

#### DIABETES MELLITUS

FIGURE		PAGE
1. Chart showing contrast between the blood-sugar curve in a normal individual and that of a diabetic . . . . .		73
2. Chart showing increase in non-volatile acid and corresponding decrease of carbon dioxide in acidosis, as compared to normal blood . . . . .		91
3. History form for diabetes mellitus . . . . .		105-108
4. Blank for patient's dietary . . . . .		119

### CHAPTER VII

#### DIABETES INSIPIDUS

1. Diagram of pituitary gland . . . . .	136
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### CHAPTER VIII

#### RICKETS

1. Deformities in rickets . . . . .	146
2. Rachitic deformities . . . . .	150
3. Rickets . . . . .	151
4. Skull in rickets . . . . .	153

### CHAPTER X

#### INFANTILE SCURVY

1. Characteristic attitude in scurvy . . . . .	183
2. Thickening of cortex of humerus from subperiosteal hemorrhage in infantile scurvy . . . . .	184
3. Thickening of cortical shadow of femur from subperiosteal hemorrhage in infantile scurvy . . . . .	185

### CHAPTER XII

#### PELLAGRA

1. Pellagrous dermatitis on back of hand . . . . .	218
2. Pellagrous dermatitis on hands and feet . . . . .	219
3. Pellagrous dermatitis on genitalia . . . . .	221



## SECTION XIV: DISEASES OF THE NERVOUS SYSTEM

## CHAPTER III

## TUMORS OF THE SPINAL CORD

1, A. Diagram of sensory innervation by segments, anterior . . . . .	340
1, B. Diagram of sensory innervation by segments, posterior . . . . .	341
2. The relation of the segments of the spinal cord and their nerve- roots to the bodies and spines of the vertebræ . . . . .	342
3. Chart of sensory disturbances in Case II . . . . .	344
4. Chart of epieritic and protopathic sensibility in Case II . . . . .	345
5. Chart of thermal sensations in Case VI . . . . .	356
6. Chart of pain sensation in Case VI . . . . .	357
7. Pain and thermal sensations in Case VIII . . . . .	364
8. Chart of sensory disturbances in Case XI . . . . .	377
9. Chart of sensory disturbances in Case XII . . . . .	385

## CHAPTER IV

## DIAGNOSIS AND LOCALIZATION OF BRAIN DISEASES

1. Hemorrhage in the prefrontal lobe following trauma . . . . .	398
2. Tumor (round-cell sarcoma) wedged in between the left frontal insula and temporal lobes, penetrating the lateral ventricle . . . . .	400
3. Glioma of the parietal lobe destroying the lenticular zone and pro- ducing paraphasia . . . . .	406
4. Motor centers . . . . .	416
5. Optic centers and tracts . . . . .	425
6. Tumor in the left basal ganglia . . . . .	432
7. Hydrocephalus, showing extensive dilatation of the cerebral cavities . . . . .	452
8. Hydrocephalus, showing characteristic contour of the head . . . . .	454
9. Primary intraventricular hemorrhage . . . . .	461
10. Aeromegaly . . . . .	464
11. Tumor of the hypophysis . . . . .	466
12. Case of bulbar palsy with involvement of the seventh, tenth and twelfth nerves . . . . .	475
13. Tumor of the vermis . . . . .	489
14. Cerebellar asynergy . . . . .	491
15. Tumor of the pontocerebellar angle . . . . .	496
16. Abscess in the right frontal lobe . . . . .	529
17. Porencephaly (feeble-mindedness; epilepsy) . . . . .	535
18. Infantile cerebral hemiplegia . . . . .	536
19. Diplegia (Little's disease) . . . . .	538
20. Little's disease . . . . .	539
21. Microcephaly and diplegia (idiot) . . . . .	540

## CHAPTER V

## APOPLEXY

1. Hemorrhage in the internal capsule . . . . .	556
2. Softening of the entire left internal capsule . . . . .	559
3. Case of right hemiplegia . . . . .	562
4. Extensive meningeal hemorrhage over right parietal lobe . . . . .	585
5. Thrombophlebitis of right cavernous sinus . . . . .	594

## CHAPTER VI

## ENCEPHALITIS

1. Hemorrhagic encephalitis . . . . .	600
2. Hemorrhagic encephalitis, secondary meningitis . . . . .	601
3. Case of tuberculous meningo-encephalitis . . . . .	611

# LIST OF ILLUSTRATIONS

xxiii

FIGURE

PAGE

## CHAPTER VII

### ABSCESS OF THE BRAIN

1. Acute localized purulent meningitis . . . . .	617
2. Brain abscess . . . . .	618
3. Miliary abscess of the brain . . . . .	628

## CHAPTER VIII

### BRAIN TUMORS

1. Cellular structure of glioma of the brain . . . . .	633
2. Glioma of the frontal lobe . . . . .	634
3. Glioma in the midbrain with involvement of the basal ganglia . . . . .	635
4. Glioma in the occipital lobe . . . . .	635
5. Tubercle found below the motor cortex . . . . .	637
6. Gumma of the cortex, growing from the pia mater . . . . .	638
7. Fibroma of the acoustic nerve in the cerebellopontine angle . . . . .	639
8. Fibroma of the hypophysis . . . . .	639
9. Tumor of the thalamus, extending subcortically in region of the gyrus angularis . . . . .	646
10. Secondary internal hydrocephalus in tumor . . . . .	646
11-12. Small round epithelioma of pons and peduncle . . . . .	647
13. Brain areas . . . . .	649
14. Functional areas of the cerebral cortex of the left side . . . . .	650
15. Larger tumor of the right paracentral convolution . . . . .	651
16. Tumor of the prefrontal area . . . . .	652
17. Tumor of the superior parietal convolution . . . . .	656
18. Diagrammatic sketch, showing sagittal sections through the normal brain-stem . . . . .	667
19. Large glioma of the pons . . . . .	671
20. Paralysis of right external rectus, right facial and left-sided hemitaxia . . . . .	672
21. Base of the brain . . . . .	676
22. Large tumor of the cerebellum . . . . .	678
23. Tumor of the fourth ventricle . . . . .	685

## CHAPTER IX

### DISEASES OF THE SPECIAL NERVES

1. The cervical plexus (after Cunningham) . . . . .	711
2. The brachial plexus (after Morris) . . . . .	715
3. The lumbosacral plexus (after Morris) . . . . .	738



# PRACTICE OF MEDICINE

## VOLUME IX

### SECTION XIII

### DISORDERS OF METABOLISM

#### CHAPTER I

#### GOUT

BY WILLIAM FLETCHER MCPHEDRAN, B.A., M.B.

Definition, p. 1—Etiology, p. 1—Predisposing causes, p. 1—Symptomatology, p. 3—Clinical history, p. 3—Physical findings, p. 5—Laboratory findings, p. 7—Blood, p. 7—Urine, p. 9—Tissues, p. 9—Special examinations, p. 10—Functional tests, p. 10—X-ray examinations, p. 10—Diagnosis, p. 11—Complications, p. 12—Clinical varieties, p. 12—Treatment, p. 14—Diet, p. 14—Climatology, p. 18—Hydrotherapy, p. 18—Medicinal treatment, p. 19—Radium and x-ray treatment, p. 20—Surgical indications, p. 20—Management of convalescence, p. 20—Prognosis, p. 21—Pathology, p. 21—Morbidity anatomy and functional pathology, p. 21—Circulatory system, p. 24—Respiratory system, p. 24—Genito-urinary system—the kidneys, p. 24—Physiology: uric acid metabolism, p. 25—Uric acid, p. 25—Uric acid metabolism in diseases other than gout, p. 30—Uric acid in normal blood, p. 30—Uric acid in gout, p. 31—Theories of gout, p. 33—Historical summary, p. 35—References, p. 37.

**Definition.**—Gout is a constitutional disease, characterized by an excess of uric acid in the circulating blood, usually by arthritis, the distinguishing feature of which is a deposition of sodium biurate in the cartilages and periarticular tissues, and usually by an associated nephritis. It may be due to disturbances in purin metabolism, or to a peculiar nephritis resulting in retention of the biurate of sodium.

**Etiology.**—**PREDISPOSING CAUSES.**—*Climate.*—While climate has no known effect upon gout, it is likely that *cold and dampness*, inasmuch as they change the individual's habits of eating and drinking, are likely to produce more cases of gout per hundred thousand of inhabitants. But it is noteworthy of the British Isles that England, less cold and less damp than Scotland, has a very much greater incidence of the disease.

*Sex.*—Males are much more likely to be affected than females. In fact, it is rare in women until after the age of childbearing. Of 80 cases

collected by the French Academy, only 2 were women; and of 124 cases in St. Bartholomew's Hospital, 24 were young women. In Futcher's series in the United States, there were about 4 per cent. Women usually give a definite history of inheritance. Their immunity is supposed to be due to not having been too much exposed to excess in eating and drinking, as is the case in men.

*Age.*—Gout is rare in the young. In Scudamore's series, only 4 (the youngest eight years of age) out of 515 cases were under the age of seventeen. When it occurs in such a young individual, it is almost certainly inherited. In Futcher's<sup>1</sup> series at the Johns Hopkins Hospital, 53 out of 92 afflicted patients were between the ages of forty and sixty when first admitted to the hospital. The general statement is that the initial attack occurs most frequently in the fourth decade.

*Race.*—The white race is especially susceptible to the disease. In Baltimore, where approximately one in every four patients admitted is colored, there were only six male negroes among the 92 patients.

*Heredity.*—Heredity plays a very important part in the genesis of the disease. Among the well-to-do classes, between 50 and 75 per cent. of the individuals give a definite history showing that either or both parents had the disease. In Scudamore's series of cases, 59 per cent. gave a history of the disease in the parents or grandparents. In his hospital practice Garrod found 50 per cent., but in his private practice, where the patients' knowledge of parental conditions was greater and their general level of intelligence probably higher, he believed the disease was inherited in three-quarters of the cases. In the United States the incidence, from a hereditary standpoint, is only about 30 per cent. The daughters of gouty families may escape the disease, but they are more likely to have gouty children than are the sons. The individual who has no family history of gout may develop it, and transmit it to his children.

*Personal and Social Conditions.*—"Poor man's gout" is not a common condition in the United States—in fact, it is probable that this affection is not gout at all, but a type of infective arthritis. In England, on the other hand, conditions are different. As Osler says: "A combination of poor food, defective hygiene, and the great consumption of excessively highly malted liquors, makes 'poor man's gout' a common affliction." "Poor man's gout" is found in the United States only where these conditions obtain, that is to say, in the large cities with an Anglo-Saxon, Hebrew, or Teutonic population, drinking malt liquors, and living in slums. It is a disease of the *city*, rather than of the country—again particularly in the lower classes, because the individual in the country generally takes bodily exercise. It is a disease of *overcrowding*, and *poor hygiene*. Employees of breweries, bartenders, and delivery-men are more prone to the disease, because of their opportunities for getting malt liquors freely. Persons of large frame and good physique, with a tendency to obesity, are the ones usually affected.

In 1772, Musgrove, Huxam and Faulkner called attention to the association of *lead-poisoning* and gout, but Garrod, about 1848, was the first

to show that lead-poisoning was really a cause and a factor in the disease. He found that 33 per cent. of the gout patients that came under his care in hospital practice had at some period of their lives suffered from lead-poisoning. In Futeher's series, only three gave positive evidence of lead-poisoning. The method of infection with lead is not known. Garrod found that the blood of patients suffering from lead poisoning contained excessive amounts of uric acid, but he also pointed out that these patients were liable to develop chronic nephritis, and drew the conclusion that the increased amount of uric acid in the circulating blood resulted from a renal insufficiency. The majority of subsequent investigators have agreed to this hypothesis, and it is probable from Pratt and McClure's recent work that this contention is really justified.

*Mental work, over-exercise, or strain* may produce an attack. A marked tendency of the big toe joints to be affected is believed to be due to ill-fitting shoes.

*Alcoholism.*—Among the "predisposing" causes, it is probable that alcohol is easily the first. The majority of people who over-eat partake of too much alcohol, and are apt to do so steadily. The fermented liquors—port, sherry, beer and ale—are much more likely to give rise to the disease than the distilled, among which are whiskey, brandy, rum and gin. The cause for the difference is, so far, unknown. It is not due apparently to the difference in the content of sugar, or of saline, nor to the degree of acidity. It is thought by many, including Futeher, that the main drink which gives rise to gout in the United States is beer.

**Symptomatology.**—**CLINICAL HISTORY.**—*Acute Gout.*—The previously healthy man of middle age is awakened suddenly in the night by intense pain, generally in the right big toe joint. Several hours after, the joint is red, slightly swollen, and tender on palpation. He has moderate fever, usually as high as 101° to 103° F. (38.3° to 39.5° C.). The pain is agonizing. The sufferer almost always realizes with what he is afflicted, if he has read of the disease, or if any of his relatives have had it. He has a pain as if his joints were being squeezed in a hot vice. About morning, the discomfort generally dies down, and he may have no more pain until the next evening. But the general rule is that he feels uncomfortable, and loses his appetite during the succeeding day. The next evening the attack generally recurs. Sydenham, who was one of the learned sufferers from the disease, said: "The pain insinuates itself with the most exquisite cruelty among the numerous small bones of the tarsus and the metatarsus, in the ligaments of which it is lurking." These attacks of nocturnal pain and diurnal malaise and discomfort last for about ten days, this period constituting the "fit of the gout." The patient's discomfort, and the tenderness in the joint, increase for the first day or two, following which there is a gradual diminution in the intensity of the pain. During this time the joint has gradually become more and more swollen. It is now found to be enlarged, reddened and shiny. The veins are slightly dilated, and about the eighth day of the attack there is quite a definite edema of the affected joint. While the inflammation never goes as far as suppuration, there

may be desquamation of the skin over the affected area. There is usually involvement of one big toe in the initial attack, but both, or even other joints, may be involved as well in the first attacks. These are the cases in which the differentiation from infective arthritis is difficult. Occasionally these metatarsal phalangeal joints escape altogether, and the attack is concentrated in the tarsal joints. Then the attack of gout is of shorter duration, and the signs of local redness, swelling and edema are not so noticeable, because there is so much loose connective tissue surrounding the joint. Thus the swelling is not so tight, nor painful, as in the toe joint.

Very often the sufferer recalls, with chagrin, that he has partaken too well, if not wisely, of some dainty that he now recollects is popularly supposed to be an actively exciting cause of the disease. This remembrance adds to his difficulties, for from time immemorial the sufferer from gout has been easily enraged.

He remains quietly in his room. So great is his discomfort, and so much is it accentuated on moving, that the physician's advice to remain quiet will be heeded. He can usually be found with one foot up on a pillow. Footstools, especially arranged and padded to ease the patient's afflicted member, can still be found in many houses in England. As swelling progresses, the patient's discomfort diminishes, and he can move around freely about the tenth day.

The next attack is variable in time. As a rule, the patient will be free from attack for about two or three years. Bradford Rose<sup>2</sup> cites the history of a man who had his initial acute attack when twenty-seven years of age, and was then free for over fifty years. Such a history, while not rare, is remarkable. First of all, there is no reason to doubt the diagnosis in this case. The British physicians of the eighteenth century knew gout as well as their opportunities allowed them to. Then, too, the British habits as to eating and the drinking of alcoholic liquors were at that time, and are still, believed to cause an attack.

After an attack the patient is likely to give more particular care to his diet and general life than he has previously done. Part of his freedom from a second attack is probably due to his heeding the warning that he has received, and he is likely to take particular pains to avoid any break from the discipline of life laid down by his medical adviser or by himself.

With our recent knowledge of the relationship of gout to nephritis, it seems reasonable to believe that this régime, coupled with the increased amount of water which the individual is likely to drink, relieves the irritation of the kidneys, so that they are allowed to perform their work to a more perfect degree. Consequently the individual is in better general health, and better able to excrete uric acid.

The general rule, however, is that the next attack recurs approximately six months after the preceding attack. There is a tendency for the fits to be more prevalent in the spring and in the fall. The next attack is frequently preceded by a number of symptoms, generally referable to the digestive system. These may include loss of appetite, gas,

and acidity. Restlessness and irritability of the nervous system, or general depression, may be observed, and we may probably ascribe these symptoms to the irritation due to the retention of nephritic toxins. The attacks may recur regularly every six months, but some may be omitted, or an aberrant attack may supervene.

**PHYSICAL FINDINGS.**—In the first attack, the joint is found enlarged, red, hot, and tender. The sufferer has fever reaching as high as  $103^{\circ}$  F. ( $39.5^{\circ}$  C.). If it is the patient's second, or subsequent attack, grating may be elicited on manipulation of the joint. As the disease progresses, more and more joints are likely to be attacked, such as the knees, joints of the hand, the wrists and the elbows. The attacks may not be nearly so severe as the initial ones, and the condition may be described as "chronic gout." In the latter case, recovery from the paroxysms becomes less complete, the recurrences are more frequent, the man's general health is more seriously impaired, and the discomfort more pronounced. Some joints become permanently stiffened, enlarged, and distorted. Large chalk stones make their appearance on the knuckles, the toes, and about the knees and the elbows. In the rare case of the individual who neither seeks a physician's advice, nor follows it, life becomes an almost continuous martyrdom, and the constitution is gravely impaired.

*Joints and Tissues Affected.*—In 341 out of 516 cases collected by Seudamore, gout was confined to one or both great toes. Next, the joints mentioned above are most frequently affected. The hips, shoulders, jaw, and vertebral joints are but rarely involved; but if these joints have been damaged by some previous accident or disease, they are more likely to be affected by gouty inflammation or infiltration. Early in the disease the cartilages are the only tissues likely to be affected in the joints, and in the absence of x-ray examination, actual damage to the joint structures may not be recognizable. But the deposition of sodium biurate around the joint, and in other localities, is the most characteristic finding in the disease. Deposition takes place early in the disease in the cartilage; later, the peri-articular fibrous structures are involved. But, in the long-continued disease, the deposition is not confined to the immediate joint structures; it may be found in ligaments, in tendon sheaths, and in subcutaneous tissue. It invades the synovial bursæ in the vicinity of joints, and causes enlargements, thickenings, cripplings, and deformities of the affected limbs. It is in this condition that the sufferer's limbs and extremities are so characteristic of the disease. The knobby, bulbous fingers, and distorted toes, elbows, and ankles of the gouty individual, are deformed by the presence of large masses of sodium biurate fixed in felted masses of crystallized needles. In the long-continued case, the deformity may be extreme. Masses as large as pigeon's eggs are frequent in the neighborhood of elbows and knees. When these masses come close to the surface, they may ulcerate through, and form aseptic ulcers that later become infected by the skin or surrounding tissues.

Concretions of sodium biurate are not by any means confined to the



joints and surrounding structure. When remote from joint structures, the concretions are known as "tophi"—a word derived from the Hebrew, meaning concretions. They are also known as "chalk stones," and Epstein and Sprague have shown that they consist a little over one-half of sodium biurate, and from 12 per cent. to 15 per cent. of calcium biurate. In the hog, similar deposits are found, composed of guanin. These are to be found in the muscles, ligaments, and articular tissues, as small whitish deposits. The common location for tophi is the helix, or antihelix, of the ear. Sir A. Garrod gives the following description of their formation in this situation: "The earliest appearance presented is that of a small vesicle under the skin of the helix, as if situated between it and the fibrocartilage; the contents of the vesicle are, at first, opalescent or milky, but afterwards become white and opaque, and acquire the consistence of cream. After some months, the vesicle assumes the appearance of a small, hard, white bead, closely resembling a pearl, and it may remain as such for years; but occasionally the thin skin is worn off, and the bead itself becomes detached from the cartilage, leaving only a slight indication of its presence. If the vesicle is punctured in the early state, a milky fluid exudes, which presents under the microscope the appearance of a transparent liquid, in which are floating a large number of very fine crystalline needles. If the contents are examined at a later state, the crystals are found aggregated into small bundles, and if the bead is solid, it is difficult to separate them, as they adhere strongly together, and form a closely interlaced crystalline mass." They are found in the subcutaneous tissue also; most often they are found on the extensor surfaces of the forearms, near the elbow joints, and near the patella in the lower limbs. They may be mistaken for rheumatic subcutaneous nodules. They may occur low down over the sacrum, or in the palms and soles, in the nose, and in the tarsal cartilages of the eye. Occasionally, they are found in the laryngeal cartilages, vocal cords, in the nervous system, in the sclerotic coat of the eye, and in the heart valve.

It is easily seen that between attacks of the disease the sufferer has had his joints and tissues so involved that he is never free from pain, and that he has lost a great deal of the power of mobility he formerly had in all his joints. As the synovial tissue is altered by these chalk-like deposits, creaking occurs, and this may be painful. While the earlier attacks are uniformly accompanied by fever, the latter ones are quite as frequently without any rise in temperature.

But in spite of the severe pain and discomfort the sufferer undergoes, it is noteworthy that he differs from the individual who is a victim of ordinary interstitial nephritis. Gout always affects the highly cultured of the race. Sydenham said: "More wise men than fools are victims of the affection," and this statement still holds as good now as it did in his day. The sufferer from chronic Bright's disease, without gout, does not generally retain his mental faculties or his physical abilities, unimpaired, whereas the gouty individual does remain mentally and physically normal. The distribution of the disease is remarkable. Many

cities of the United States and Canada hardly ever see it in their hospital service. Boston, New York and Baltimore are three cities where it can readily be seen in the ordinary run of the in-patients' and out-patients' departments.

LABORATORY FINDINGS.—(1) *Blood*.—The blood in acute gout is characterized by a leukocytosis that may reach as high as twenty thousand cells per cu.mm. In spite of this high count, the process never goes on to suppuration. The red blood-cells are decreased neither in number nor in their content of hemoglobin. Occasionally various writers have described conditions in the differential count of the white blood-cells that they believed to be of importance in the diagnosis of the disease, but these results have never been consistently confirmed. Garrod used to maintain that there was, in the acute attacks, a reduced alkalinity of the blood. In cases of gout complicated by lead poisoning, it is to be expected that the red blood-cells will show the changes characteristic of the lead poisoning. The main interest, in the blood, is centered upon the content of uric acid. Folin and McCallum<sup>3</sup> observed that uric acid gives phosphotungstic acid and an alkali a deep blue color that is proportional in its intensity to the amount of uric acid present. Owing to the presence of proteins in the blood, this reaction is complicated more than the similar one in the urine. It is first necessary to free the blood from proteins. For this purpose, Benedict<sup>4</sup> has suggested the use of a solution of colloidal iron.

Method.—To 20 cc. (a) of oxalated blood are added 100 c.c. of boiling N/100 acetic acid in a casserole, and the mixture is heated to the boiling point for a moment. Remove the casserole from the flame, and add 200 c.c. of boiling distilled water. Pour the mixture on a folded filter, and wash the residue with 50 c.c. of boiling water (heated in the same casserole in which the original coagulation took place). Transfer the whole filtrate to a casserole, and boil it down rapidly, until the amount is about 25 c.c. Pour this solution into a small flask roughly marked to indicate a volume of about 50 c.c. Transfer the whole contents of the casserole quantitatively to the flask, with the help of two or three washings of water, heating vigorously to boiling, and rubbing the sides of the casserole each time with a rubber-tipped stirring rod of glass. The total amount in the flask, after the addition of the washings, should not exceed 50 c.c. Thoroughly cool the turbid solution in the flask by holding it under running water, and add 2 c.c. (b) of colloidal iron solution, while the flask is being gently rotated. Filter the mixture through a small folded filter into a 100 c.c. Jena, Nonsol, or pyrex Florence flask, and wash the residue twice with distilled water. The filtrate here obtained should be clear and colorless as distilled water. Boil the solution down to a volume of from 1 to 2 c.c., taking care in the initial stage to keep the mixture from bumping, and carefully pour into a small centrifuge tube. Then rinse out the flask with successive small portions (from 1 to 2 c.c.) of water, heating each, and shaking thoroughly before adding to the centrifuge tube. Then the volume should be from 5 to 10 c.c. in the centrifuge tube. Cool the liquid, add 20 drops of the

ammoniacal silver magnesium solution, (c) and mix with a small stirring rod and centrifuge for two or three minutes. Pour off the supernatant fluid as completely as possible, drain and remove the last drop with a piece of filter paper. Add to the residue two drops of a 5 per cent. solution of potassium cyanid to dissolve up the silver urate, stir thoroughly with a thin rod, add a few drops of water, and stir again. Two c.c. of the uric acid reagent (d) are then added, and the mixture stirred again. Then add 10 c.c. of a 20 per cent. sodium carbonate solution, transfer quantitatively to a 50 c.c. flask, and after a minute dilute up to the mark with distilled water. Then compare the resultant solution in a Duboseq, or other accurate colorimeter, with a simultaneously prepared solution obtained by treating 5 c.c. of the standard uric acid solution (e) contained in a 50 c.c. flask with 2 drops of potassium cyanid solution, 2 c.c. of the uric acid reagent, 10 c.c. of the 2 per cent. sodium carbonate solution, and diluting to the mark 50 at the end of a minute. The standard solution is best set at the mark 1.0 in the Duboseq colorimeter.

Calculation.—The number, or reading of the standard, divided by the reading of the unknown, gives the number of mg. of uric acid in the specimen taken.

(a) Smaller amounts of blood may be employed, and the quantities of water and acetic acid similarly reduced. Unless the quantities of uric acid are very large, more accurate results are obtained by taking 20 c.c.

(b) The precipitate should separate out in large flocculent masses, when the right amount of iron solution is added. With old specimens of blood it may be necessary to take 4 or 5 c.c. of iron solution, and add a little 10 per cent. sodium chlorid solution. At the same time, any excess of iron would tend to oxidize the uric acid, and so must be avoided.

(c) Ammoniacal silver magnesium mixture is:

Silver lactate solution (3 per cent.)	70 c.c.
Magnesia mixture	30 c.c.
Concentrated ammonium hydroxid solution..	100 c.c.

(d) Uric acid reagent is prepared by placing 100 grams of sodium tungstate, 80 c.c. of 85 per cent. phosphoric acid, and 750 c.c. of distilled water, in a liter flask. Boil the mixture with a reflux cooler for two hours, cool, and dilute to one liter. Filter if necessary.

(e) Standard uric acid solution: The solution of uric acid in phosphate solution is readily prepared. It does not need to be standardized, and keeps perfectly. Nine grams of  $\text{NaH}_2\text{PO}_4$  and 1 of  $\text{NaH}_2\text{P}_2\text{O}_7$  (both pure, and recrystallized) are placed in about 300 c.c. of hot distilled water, and the solution filtered if not clear. This solution is made up to 500 c.c., and poured upon exactly 200 mgs. of uric acid suspended in a few c.c. of distilled water in a liter flask. The phosphate solution must be perfectly clear. Shake the flask until the mixture is quite clear, and the uric acid is dissolved. Cool, and add exactly 1.4 c.c. of glacial acetic acid, dilute to the mark, and mix well. Then add about 5 c.c. of

chloroform to prevent the formation of molds. Five c.c. of the solution contains 1 mg. of uric acid.

Folin and Denis<sup>5</sup> found that the average amount of uric acid in the normal individual, on a purin-free diet, was from 1.5 to 2.5 mm. per 100 c.c. Studies made since their original paper make it probable that the amount in normal individuals may even go as high as 3 mm. per 100 c.c. But if this amount is exceeded on a purin-free diet, particularly if the amount of non-protein nitrogen remains low, it is very good evidence of gout. This is so, even if there are as yet no joint or connective tissue manifestations of the disease.

(2) *Urine*.—During the acute attack of gout, the urine will be reduced in amount, high in specific gravity, and may contain a little deposit. This was said to be of urates, or uric acid crystals. It is not likely that the deposit is uric acid, because the amount of uric acid excreted in the urine is diminished at the onset of an attack. Usually, there is a trace of albumin, a few finely granular or hyaline casts, and may be some epithelial cells. Normally, the amount of uric acid excreted per day is about from 0.7 to 1.0 gram, on a normal varied diet, and from 0.35 to 0.45 gram on a purin-free diet. For three or four days before the attack comes on the amount of uric acid will be reduced to the lower normal limit. With the third or fourth day of the attack, the amount usually rises to about the upper limit of the normal, that is to say, to 1.0 gram. The individual has a normal excretion of uric acid per day. This does not vary much from day to day, but there is a great variation in the figures of normal individuals. The amount of phosphoric acid excreted is usually proportional to the amount of uric acid.

In the chronic form of the disease, or in between attacks, the character of the urine is that of chronic interstitial nephritis. The amount is increased up to about 2 liters per day, and there is a marked increase in the amount passed between 9 P. M. and 7 A. M. There are hyaline and finely granular casts, and a trace of albumin. Even more noticeable deviations from the normal will be found on performance of the tests for kidney function. The excretion of phenolsulphonephthalein is low, the water test is delayed, and the urine is fixed in specific gravity.

When one reflects upon the varied origin of uric acid, and the multiplicity of ways in which its metabolism may be altered in the body, one sees how ridiculous it is to draw any conclusions from the amount of urates found in the urine.

Estimation of uric acid in the urine: From 2 to 4 c.c. of urine (the amount that will contain about from 0.7 to 1.3 mgs. of uric acid) are placed in a centrifuge tube, and diluted to 5 c.c.; 20 drops of the ammoniacal silver magnesia solution are then added. The procedure is then the same as that of the uric acid estimation in the blood.

(3) *Tissues*.—In many cases there is considerable doubt as to the identity of the disease. The individual may have little hard lumps upon the helix of the ear, and still show no signs of joint inflammation. In these cases, it is important to make a decision, for therapeutic purposes,

and no better way has been devised than to open one of these little tubercles with a needle and examine the contents. In the case of gout, one finds large numbers of the crystals. They are needle-shaped, pointed, and generally colorless. The minute swellings with which tophi may be confused are the Darwinian tubercle, small fibroid nodules on the margin of the ear, and small sebaceous cysts. The latter is the only swelling that is likely to give rise to real confusion, and the findings of epithelial cells, and fat droplets, readily differentiate the two when opened and put under the microscope.

**SPECIAL EXAMINATIONS.—*Functional Tests.***—It is evident from the recently acquired knowledge of the relationship of gout to chronic interstitial nephritis, that the sufferer from gout should have his renal functional efficiency tests done at the earliest moment. From them much information may be acquired as to his real status. As a first test, the phenolsulphonephthalein test of Rowntree and Geraghty may be carried out. This will roughly classify the patient's condition. Other tests that will give even more information are those showing the patient's ability to concentrate urine; and the water test, which estimates the amount of water that he will excrete when given a definite amount on an empty stomach, the excretion to be concluded at the end of four hours. Then the nitrogen, both non-protein and urea of the blood, may be examined. Unless a careful metabolic study is made, it is unlikely that much information will be derived from the study of the uric acid of the urine. But, if he is put on a purin-free diet for several days, and the uric acid of the blood measured by the methods outlined above, a great deal of information may be acquired. First of all, we may satisfy ourselves that he is, or is not, suffering from gout. We should be careful, however, to avoid deriving any satisfaction from the actual amount of uric acid found in his blood, for there is definite reason to believe that the amount of uric acid in the blood has little to do with the frequency or severity of the joint manifestation. The work of Pratt and McClure<sup>6</sup> on the relationship of uric acid to gout, and of gout to renal disease, would make one sure that little was to be derived from estimating the amount of uric acid in the blood of an individual, and then feeding him a meal of sweetbread. It is hardly desirable to give him a large amount of sweetbread, or other nuclein-containing material to eat in order to see whether it promotes an attack, because we realize that every attack is fraught with the possibility of increased damage to the kidneys.

Fine<sup>7</sup> has also drawn attention to the persistency with which one observes high uric acid figures in the blood early in nephritis. He points out that uric acid is one of the first substances to be retained by the kidneys in nephritis, and urges, when a high per cent. of uric acid is found in the blood, that all possible steps be taken to prove into which category the individual may be placed—as suffering from nephritis or from gout.

**X-ray Examinations.**—One would expect from the involvement of bone cartilage and periarticular tissues with such hard masses, that the

*x-ray* examination would be of great benefit in the diagnosis of gout. However, this is not true in the great majority of cases of the disease. The biurate of soda does not give a sharp shadow upon the plate—it is almost translucent to the ray. Consequently, except for the thickening of the soft tissue around the joints, there is very little to be found in the screen, or even plate examination. Naturally, these large deposits of urate in the tissues are only found in the old chronic cases wherein there is little possibility of doubt as to the diagnosis. In the initial stages of the disease, the depositions are so small in amount that the ray penetrates the tissues without any difficulty. One of the commonest findings in the late disease is a curious punched-out appearance, whether in the articular surfaces of the terminal phalanges, or in the shaft of the phalanges themselves. This has the appearance of a small pea that is quite translucent to the ray; it is due to the fact that the bone structure is absorbed, and then the vacancy filled in with urate deposits. Christian<sup>a</sup> draws attention to the possibility that this punched-out appearance in the articular surfaces, or in the shaft of the bones, is due to chronic poly-arthritis, which is, of course, not gouty in character. The evidence from roentgen ray examinations is negative, rather than positive, in gout. Cases that are difficult to differentiate from gout are more likely to show changes in the plate than if they were gout.

**Diagnosis.**—In ordinary cases of gout there will be little difficulty in establishing a correct diagnosis. The three diseases from which it must be differentiated are osteo-arthritis, rheumatic fever, and, in the early stages, nephritis.

Careful inquiry as to heredity, habits of eating and drinking, occupation, and general habits of life, particularly as to exercise, are of importance. The physician should carefully examine into the possibility of there having been earlier attacks, no matter how remote they may have been. The occurrence of an attack, or series of attacks, not accompanied by fever, but characterized by severe pains in the joints, should arouse the suspicion that the disease is gout. Significant factors, such as the family history, habits of life, and the location of the pain in the great toes, would indicate that the previous illnesses were attacks of gout. The suspicion is even more strongly upheld should the patient report that he had symptoms which suggest chronic interstitial nephritis. Now-a-days, it is difficult to obtain a confession of excess in eating or drinking, for the war, and also the effort that has been made to popularize a knowledge of preventive medicine and hygiene, have led the public to consider these practices not only inadvisable, but also unfashionable. The inquiries should therefore be explicit.

It is important to ascertain the age at which the first attack was experienced. Gout is unusual before the age of thirty-five years; chronic inflammatory lesions of the joints have usually established themselves by that time. Males are more likely to have gout than females. The reverse is true of osteo-arthritis. With chronic infective arthritis, there is often a history of symptoms indicating embarrassment of the cardiovascular system, as in chronic rheumatic fever, or of some remote infection, such

as of the tonsils or teeth (in osteo-arthritis), that has led to the trouble seated in the joints.

In gout the fever is not so high, while the local pain is more severe. The larger joints, except the knees, are not so apt to be involved as in arthritis, and one hardly ever finds any pain in the vertebral joints—a common seat of trouble in osteo-arthritis. As the attack of gout subsides, the edema is remarkable. This is not observed in infections.

The deformity produced in each disease is characteristic in most cases. In gout, it will be remembered, the lesion consists in irregular, hard, whitish, cherry- or grape-like masses which protrude out of the tissue. In infectious arthritis the joints are often fusiform, rounded, smooth, and without prominence. There is generally an excess of fluid in the joint. X-ray examination will usually disclose the abnormality of form in infectious arthritis. Here, too, is to be found marked ulnar deflexion of the hand, and atrophy of the interosseous muscles. Heberden's nodes are frequently observed.

Care should be taken in all cases of arthritis to examine the ears for tophi. Many will be found, if sufficient time is taken to look for them. If a suspicious tubercle is found, it is a simple matter to open it and examine the contents.

In the differential diagnosis between osteo-arthritis and gout, mention should be made of the therapeutic test. Gout is often relieved by careful dieting, by colchicum, and by atophan. Osteo-arthritis may be relieved by salicylates, gout but rarely.

There is great difficulty in establishing a diagnosis between acute gout in the initial stage and nephritis. Careful search should be made for the primary source of infection, for we must remember that nephritis is rarely primary.

**Complications.**—*Cardiovascular.*—Cardiovascular arteriosclerosis is extremely common. In fact, it is rare in an autopsy to find a sufferer from gout who does not show a marked thickening of the aorta and arteries. The distribution of the thickening is generally universal all over the body, and the intima is mainly involved. The kidneys, and the vessels of the intestinal tract, are particularly affected. Because of the extra work imposed upon the heart by this sclerotic process, hypertrophy and dilatation of the left ventricle are common. This hypertrophy and dilatation may result in irregular heart action, edema, and swelling of the liver. Not only may enlargement of the heart be noticeable from hypertension, but, as the mouths of the coronary vessels are easily occluded, there may be localized degenerations of the muscles. Thus attacks of angina pectoris, phlebitis, and venous thrombosis are quite often found.

*Renal.*—While chronic interstitial nephritis and smallness and granulation of the kidney used to be ascribed to gouty origin, it is probable that the nephritis is part and parcel of the gout, rather than a complication.

**Clinical Varieties.**—**ABERRANT TYPES OF GOUT.**—One hesitates to include under this heading any detailed description of symptoms popularly supposed to be gout, or rather of the gouty diathesis. It is regret-

table that when the patient has never had any previous gouty articular attacks, many physicians, unable to solve the cause of the malady, often describe it as due to the "gouty diathesis" or "too much uric acid in the blood." These patients keep large numbers of health resorts full all over the country. Here they live a regular life, are away from their usual surroundings, and are also, it must be confessed, humbugged. In many cases, the diagnosis of gout is made by the physician when he finds a deposit of uric acid, or urates, in the urine. The source of production of uric acid is varied, and whether it comes from the food, from the wear and tear of the cell nuclei, or from the free hypoxanthin of the muscles, its metabolism may be disturbed by exercise or fever. In view of these facts it is inadvisable to attribute to uric acid, in the absence of definite signs of gout, any malign influence. The symptoms of which these patients complain are generally referable to the nervous system. They have a good rest, and something to occupy their minds, until they make another trip to the same or a different health resort.

However, there seems little reason to doubt that there are many sufferers from gout, who, between attacks, suffer from disturbances, and show symptoms which are not arthritic. As a general rule, the individual enjoys perfect health between attacks. Occasionally, these symptoms may be prominent, and may be premonitory of an attack of acute articular gout. Generally, however, they are not connected in any way with the paroxysms.

Similar diverse signs may be found in people who have never had any regular articular paroxysms. In general, these symptoms are found in those whose parents, or grandparents, have had the disease. While the daughters usually escape, they may transmit it to their children. One son may have articular attacks in spite of his efforts to abstain from food and drink known to promote paroxysms, while the other son, who escapes the joint symptoms, may have evidences in other parts. These manifestations are to be considered gouty, because the patient probably suffers from chronic nephritis, and because they yield often to the treatment most commonly advocated for the usual articular form of the disease.

**GOUTY AFFECTIONS OF THE SKIN.**—Cutaneous affections are frequently found in the gouty. The most distinctive is eczema, usually of the external ear, and of the parts in that immediate neighborhood. The eczema is not severe, but very persistent. It usually starts on the ear, and spreads to the face, forehead, and back of the neck. Occasionally it becomes serious, especially in older people, who are unable to sleep because of the irritation. Psoriasis may be found; indeed, in elderly patients who have not been troubled with this lesion in youth, psoriasis should always raise in the physician's mind the possibility of gout. Pruritus may be very distressing.

The **NAILS** are often affected. They may be fluted, or scored vertically, or become brittle and difficult to keep in order.

**DIGESTIVE SYSTEM.**—The digestive system often suffers in this malady. Very frequently the symptoms may depend upon constipation caused



by the patient's diet, which does not comprise enough residue to keep the bowels moving freely. In addition to this constipation, he is apt to suffer from the retention products, and from nephritis.

**THE EYE.**—The most peculiar of the eye affections are conjunctivitis and scleritis. Garrod once found deposits of sodium biurate in the sclerotic coat.

**NERVOUS SYSTEM.**—One finds depression, headache, migraine, and sciatica. These are, however, very likely due to the accompanying nephritis.

**Treatment.**—As nothing is known with certainty as to the actual exciting cause of gout, the treatment employed must be largely empirical and symptomatic. In families in which there is a history of hereditary gout, great care should be taken of the children, to lessen the probability of their developing the disease. One finds here a condition which has much in common with those that are being developed by Allan, Joslin, and their schools in the United States, in the treatment of diabetes mellitus. The general consensus of opinion is that the ideal weights, as published by insurance companies, are too high, and that the vast majority of individuals eat and drink far too much, when one considers their grade of physical and mental activity. The patient who has a history of gout in his family should **live temperately**, drink almost **no alcoholic liquor**, and eat just enough to prevent his body weight from increasing. He should keep to the lower limit of caloric intake, rather than the medium or high limits. Also he should devote a regular portion of his time to **recreation out of doors**. Golf, tennis, horseback-riding, and any winter sports are suitable. He should be advised not to develop the motor car habit, but to walk to and from his business daily. At the same time care must be taken, should an attack already have affected the patient, not to produce others by over-exercise and fatigue.

During the winter months, in case the patient is unable to enter into winter sports such as skating, skiing or tobogganing, the various systems of **indoor gymnastics** may be tried out to advantage. Probably the best of these is Müller's system. This has the particular advantage of being designed to exercise the abdominal muscles, and by doing so it improves the digestion and general feeling of well-being. It is hardly necessary, nowadays, to advise the patient to take a **bath** daily. If he is too stout, and has no serious heart lesion, very warm baths, followed by massage, or a Turkish bath, will be of benefit in reducing weight, or in increasing his oxidative processes. Chills should be avoided, also exposure to wet and cold.

**DIET.**—It is by careful regulation of the food intake that the most progress can be made. Undoubtedly, **meat** is the one article to which clinical experience attributes the **malignant influence**, but it is noteworthy that controversy has raged over the kind of meat that is most injurious, without any definite result having been attained. Custom attributes to the red meats the greatest injurious power, but Kaufmann and Mohr have shown that there is very little difference between the kinds of meat, so far as the purin is concerned.

Von Noorden and Umber, two of the best German students of dietetics in relation to gout, recommended that the determination of the purin-tolerance of each individual be ascertained by giving him, after several days of a purin-free diet, a definite quantity of meat, and noting how promptly he excreted the purin derived therefrom. He was then to be put on a diet, the purin of which he could excrete easily. Umber, in addition to this procedure, advocated that the individual entirely abstain from purin for several days of the week, in the hope that he would eliminate the surplus from the other days, and so avoid an attack. It is probable that this procedure, involving as it does a great deal of work on the part of patient, nurse, and physician, is not of much importance, for Pratt and McClure have shown recently that retention of purin-content food is not significant of gout, and that it is found in many other illnesses, or even when the individual is in a healthy state. A diverse diet, low in caloric intake, is probably superior to the unrestricted purin-free diet.

At the same time, the protein foods particularly to be avoided are those rich in cell nuclei, which contain an abundance of purin bodies. These are: sweetbreads, liver, kidney, and brains. In addition, meat extracts of all kinds, both the commercially prepared and meat soups, are to be avoided. The meat extracts are undesirable, not only because of their richness in nitrogenous extractives, but also because of their high content in sodium chlorid. For the same reason salt-fish should be avoided. Fish and chicken are still the main basis of the protein diet of the well-to-do, but they probably give as much purin output as ordinary meats, in proportion to their weight.

**Eggs** are the most valuable protein for gouty patients. Eggs and **milk** are always easily obtainable; they can be had fresh at any time of the year, are purin-free, and with modern cookery are capable of much variation. **Cheese** is also easily obtainable, and is very desirable. It may be combined into various attractive dishes with eggs and milk.

Any **starchy food** may be used freely. Bread, rice, potatoes, and any green vegetables should form the major portion of the dietary. It is improbable that the vegetable albumins so widely and commercially developed by the Germans are of any use.

A good deal of nourishment, not usually taken into consideration, may be derived from **fruits**, particularly from oranges, pineapple and grapefruit. It is known now that the acid combinations in these fruits are oxidized into carbonates, and that consequently the acid is no obstacle. In a few instances bananas or strawberries may cause joint pains. In these cases their use should be restricted.

**Seasoning** is, naturally, to be avoided. The one fact of which we are now sure in regard to gout, is that there is kidney involvement in a very high percentage of the cases, and anything that tends to diminish the function of the kidneys should be omitted from the dietary. In addition to this restriction, anything that is difficult to digest should be taken in small amounts. In the United States and Canada, par-

ticular mention should be made of pickles, vinegar, and highly salted foods. Not only are they difficult of excretion by the kidneys, but they interfere with digestion. Eating between meals is also inadvisable, because of its tendency to upset the digestion.

It will be seen that the individual's diet must be considered rather than the disease. While ten years ago it was customary to limit unduly the consumption of protein foods, latter day experience tends to show that a reduction of the caloric intake, rather than of the purin, is necessary.

The writers of the last century paid a great deal of attention to the kind of **alcoholic beverages** of which the sufferer of gout might safely partake. Fortunately, the present trend, through moderation, to abstinence, is doing a great deal to settle the matter of alcoholic beverages. The physician can confidently recommend his patient to abstinence, for the latter experiences better health, and is much less likely to be afflicted with an attack, if he follows this advice. The fermented beverages are the most likely to cause an attack. One frequently meets patients who dine out regularly, and have attacks only after taking wine or beer. Not infrequently the attack comes on within two or three hours after the indulgence.

Should alcohol be indicated, as doubtless it is in middle-aged or elderly individuals with heart disease, who lack bodily vigor, the distilled drinks do much less harm than the others. Whiskey, or brandy, may be fairly safely prescribed. It is noteworthy that the nations consuming the stronger distilled drinks do not show nearly so high a percentage of attacks as those using the fermented liquors. Gout, for example, is very rare in Scotland, and very common in England. Of the wines, port, sherry, madeira, and champagne, and ales, stout and beer, when high in percentage of alcohol, are the most likely to promote an attack. Mild native wines and 2 per cent. beer are fairly safe.

**Tea, coffee and cocoa** were eliminated from the diet by physicians of the nineteenth century. This elimination found scientific confirmation in Fischer's discovery that they belong to the purin group. But in their constitution is a methyl group, and there seems little doubt that the methyl purin, on digestion, breaks down the uric acid. Consequently, if there is no contra-indication, these beverages can be indulged in fairly liberally.

During the gout attack, diet is very important. It should be as nearly purin-free as possible, small in amount, and include at least three liters of fluid a day, unless the patient suffers from heart disease, in which case the amount should not be greater than two liters. For the first day or two, when the fever is high, the patient should take nothing but milk—200 c.c. (1 glass) with lactose 4 drams (1 teaspoonful) every two or three hours. As the symptoms gradually abate, eggs, butter, white bread, rice, tapioca, and cheese should be added to the diet; and when the fever entirely disappears, he may take small amounts of white fish, chicken or other fowl. A good purin-free test-diet is as follows:

## PURIN-FREE TEST-DIET\*

*Breakfast:* Fruit, 250 grams; milk, 250 c.c.; one roll.

*Dinner:* Pudding (consisting of 100 grams wheat flour, 150 c.c. milk, 3 eggs, and 50 grams butter); 200 grams stewed fruit.

*Supper:* Cereal (consisting of 50 grams meal, 750 c.c. milk, 20 grams sugar); fruit (raw or stewed), 250 grams; one roll; butter, 50 grams.

During the day a liter of water should be taken in addition to the fluids of the above diet.

The following lists may be helpful to the practitioner in dealing with cases of gout:

## PURIN CONTENT OF FOODSTUFFS

## A. Purin-free foods, containing no purins or only traces of it:

Bread, cereals (oatmeal, rice, sago, tapioca, etc.); fruits (bananas, pineapples, peaches, grapes, pears, plums, cranberries, oranges, apricots, huckleberries; apples); nuts (walnuts, hazelnuts, almonds); certain vegetables (cucumbers, cabbage, turnips, onions, tomatoes); milk, cream, butter, certain cheeses (Edam, Swiss, Gervais, Roquefort); eggs.

## B. Purin-poor foods, containing only small amounts:

Certain cheeses (cream cheese, ordinary American cheese); caviar; certain vegetables (lettuce, radishes, cauliflower, celery, asparagus, string beans, potatoes, carrots).

## C. Purin-containing foods:

Meats (beef, veal, mutton, pork, tongue, brain, chicken, goose, venison, fish, oysters, crabs, lobsters); certain vegetables (spinach, kohlrabi, peas, beans).

## D. Foods extremely rich in purins:

Sweetbreads, liver, kidney, herring, sardines, anchovies.

Bouillon is rich in purins; beer contains considerable nucleic acid from yeast; coffee, tea, chocolate and cocoa contain methylpurins, but they do not give rise to uric acid.

For making tests requiring a purin-free diet, a sample diet has already been given. In addition, the following meals may be found convenient:

*Breakfast:* Coffee (decaffeinated) with cream, toast, butter, marmalade, eggs, milk.

*Dinner:* Vegetable or cream soup (no meat or meat extract), potato, vegetable from list A with butter, stewed fruit, rice, sago, or tapioca pudding.

*Supper:* Omelette, or scrambled eggs, cheese, bread and butter, fruit, milk (hot or cold).

\* From Barker's "Clinical Diagnosis of Internal Diseases."  
VOL. IX.—2.

**CLIMATOLOGY.**—The patient who can go to a **dry, fairly warm climate**, where his perspiration will be stimulated, and consequently his intake of water increased, will receive a great deal of benefit therefrom. In spite of the absence of infection in the joint, many patients experience twinges upon the advent of bad weather. Such a patient will undoubtedly be benefited by a sojourn in the South during the winter and fall.

If the joint has a small amount of connective tissue around it (for example, the great toe joint as opposed to the ankle or shoulder joints) much can be done to comfort the sufferer during the attack. **The affected portion should be elevated** to the level of the body, and **wrapped up** in thick *layers of raw cotton*, surrounded by silk. This method preserves the local heat of the joint, and induces local sweating and swelling. It is a common experience that the pain diminishes as the sweating and swelling increase. Should the individual derive benefit from **local heat**, or from **cold**, they may be applied either by a hot water bottle, electric pad, or coils of ice water. Several English physicians feel that the application of cold is not free from danger, because of the possibility of causing disease in the internal organs, by the reduction of the local processes. More strenuous local measures, such as blister-raising or Paquelin's cautery, are inadvisable. Various **lotions**, such as laudanum and water, or whiskey and water, may give relief, and ichthyol, belladonna and glycerin, or ichthyol and laudanum, have been recommended. Occasionally, the application of high temperature, by baking in an electric oven, may produce some effect.

**HYDROTHERAPY.**—Undoubtedly the patient ascribes a great deal of the benefit he receives from visits to Cures to the **hydrotherapeutic, mechanotherapeutic, and massage treatments** that he undergoes there. It is doubtful whether much actual improvement in the local or general conditions is really to be ascribed to these measures. Without question, the general circulation is improved, and with it the nutrition of all the parts affected. Alkalis have been highly recommended in the treatment of gout, because it was supposed that they rendered the reaction of the blood more alkaline, and in addition rendered the uric acid combinations of the blood and joints more soluble, and so more readily excreted. We know, however, from the studies on the hydrogen-ion content of the blood under various conditions, how impossible it is to change the reaction of the blood by the administration of various remedies. **Lithium carbonate and citrate** are very frequently used—5 grains (0.324 gram) dissolved in a tumbler of water, and taken from four to six times a day. We know how difficult it is to induce a patient to drink water during any illness. This difficulty is greatly increased when the illness is chronic for several years. The reason the individual drinks the water is that he notices a taste, and either drinks more water to get rid of the taste, or else feels that the constituent causing the taste is doing him some good. Undoubtedly the good effect comes mainly from the quantity that he imbibes. Were it possible to get him to drink water as freely at home, and to take as much care of himself at home as at an institution, he would probably do as well

in his own surroundings on a modified diet if he were free from business worries, and had artistic or other entertainment.

**Mineral springs** are situated all over the country, and wherever they are, usually claim to benefit gout. Probably the best in the United States are Saratoga, White Sulphur Springs, Virginia, Waukesha, and Preston in Ontario; in England, Buxton and Strathpeffer; in France, Aix-les-bains and Contrexeville. Undoubtedly, the greater part of the improvement comes from the regular régime of these places, and from the fact that the patient is willing to do as he is told. It is claimed that passive movement of the defective joint, as soon as it can be borne, is efficacious. As long as it is painless, it is probable that the circulation is improved thereby, and consequently the local functions.

**MEDICINAL TREATMENT.**—Of all the drugs that have been advocated for gout, **colchicum** is probably the satisfactory single remedy. It should be given as a wine in 1 c.c. (16 minim) doses, every two hours for four doses, and then every four hours until the pain is relieved. Usually, this relief follows rapidly, and as soon as effected the colchicum should be discontinued at once, because it is not known to have any direct action on the gouty processes, and it may cause harm. Other than relief from pain, the symptoms to be watched for are vomiting, purging, and cardiac depression. Naturally, the appearance of any of these should cause the immediate discontinuation of the drug. Should digestive disturbances appear, small doses of **opium**, such as **Dover's powder**, 0.3 gram (5 grains) may be used, and should there be any signs of heart depression, **strophanthin** 0.00065 gram, or 1/100 of a grain, may be given intravenously, followed by the administration of 1 c.c. (16 minims) of **tincture of digitalis**, four times a day. Should the depression be very serious, **ether** 4 c.c. (1 fluid dram) can be given intramuscularly. The colchicum may be replaced by its active principle, **colchicin**, in doses of 0.003 gram (or 1/20 of a grain), used exactly as above. **Salicylates** often succeed in gout where colchicum fails, even in the absence of any history of rheumatic infection. **Acetyl salicylate** (aspirin) from 0.6 to 1.3 grams (9 to 20 grains) every two or four hours is a good preparation, because it is unlikely to be accompanied by any depression or nausea. Should there be any contra-indication to the aspirin administration—that is to say, should the patient have any idiosyncrasies against taking it—it may be replaced by **sodium salicylate** in double the dosage, combined with three times the dosage of **sodium bicarbonate**. **Acetphenetidin** (phenacetin) or **antipyrin** in doses of 0.3 gram (5 grains) have been used in many cases. It is doubtful whether they are advantageous. The greatest caution should be used both in the case of the salicylates, and in that of the latter two drugs, when the patient has high blood-pressure or cardiac disability. All drugs should be taken in water, or be followed by it, and the patient may profitably be directed to lie on his right side, so as to secure as early a discharge from the stomach as possible.

**Atophan** (2 phenylchinolin—4 carbonic acid) and its substitutional product, **novatophan**, has been given with marked success, in doses of

0.5 gram ( $7\frac{1}{2}$  grains) from four to six times a day. It lowers the retaining power of the kidney so that more uric acid is excreted, and less is found in the blood after its administration. Its greatest effect is reached in one day; administration after two days is of no use. There is little reason to believe that the uric acid is "mobilized" from the joints, as epinephrin is supposed to mobilize sugar from the glycogen contained in the liver. It should be given in courses of two days, between attacks. Occasionally a threatened attack may be aborted, because the uric acid excretion is then at its lowest level. The drug should not be given during an acute attack, because the uric acid is already being excreted as rapidly as possible.

The effect of atophan on the excretion, and the decrease of the uric acid in the blood, begins directly after the absorption of the drug has taken place, and reaches its maximum in one day. Further use of the drug in greater than the usual dose per day—from 3 to 5 grams (46.3 to 77.1 grains)—is not followed by any effect. After the drug is discontinued there is a marked fall in the output, and a return to the earlier figure in the blood content corresponding to the initial reduction.

Denis found that aspirin and sodium salicylate, administered in the same large doses that are used in rheumatic fever, are capable of causing large decreases in the uric acid content of the blood. When the percentage of non-protein nitrogen is high it is also reduced. This lowered value of uric acid is due to a lowered threshold value for the kidney. **Benzoic acid** increases the uric acid excretion, and lowers the blood content, when administered in doses of from 5 to 8 grams (77.1 to 123.5 grains) per day.

**RADIUM AND X-RAY TREATMENT OF GOUT.**—Certain of Gudzent's experiments on the effect of radium emanations on the solubility of sodium biurate gave rise to the hope that the deposits in the various areas might be relieved by raying, either with radium or with a high power x-ray. It was hoped that the treatment might render the deposits more readily soluble, and thus remove the infiltration from the tissues. Fine and Chase<sup>9</sup> have shown that radium, administered both internally as a bromid and externally as an emanation, had no effect upon the lesions, or upon the uric acid content of the blood or urine.

Bain<sup>10</sup> found that the calcium metabolism was disturbed in gout, and that foods rich in **calcium** restricted the uric acid output. Hence, in his opinion, this should be kept at as low a level as possible. Were this theory carried out, milk would cease to be the favorite remedy that it is.

**SURGICAL INDICATIONS.**—Should topi be observed ulcerating through to the skin (now only in rare cases), surgical intervention may be required. As much as possible should be removed, and moist compresses, either of **sodium hypochlorite**, **Dakin's solution**, or **boracic acid**, should be applied daily until the part is free from suppurative discharge.

**MANAGEMENT OF CONVALESCENCE.**—In convalescence, the patient should be warned against adding to the diet, except by slow degrees.

Probably a short cure at a spring will be beneficial to him, because he will see how other individuals live who are afflicted with a metabolic disease.

**Prognosis.**—Once gout has made its appearance in an individual, it is unlikely that he will ever be completely free from its grasp. Attacks are likely to recur at intervals of one year, or six months, for the rest of his life, unless he diets with care. Occasionally, as in the case of the famous Yorkshire squire cited by Rolleston, the second attack may follow the first one at an interval of forty or fifty years. But this type of the disease is rare. This long interval between attacks may be due to treatment, and to the careful régime under which the patient lives. But it may happen spontaneously, without any change in the patient's life. A fatal termination from gout, per se, is not common. Death may ensue in cases of the so-called metastatic, or retrocedent gout. But as long as the individual continues to have exacerbations of his arthritis, it is unlikely that one can predict a shortening of his normal expectation of life. It is only when the disease diverges from the normal that affections of the internal organ are apt to be prominent. The fatal terminations in gout are usually due to uremia, myocarditis with dilatation, or to pericarditis. We are cognizant of the fact that all these changes are to be found with nephritis. As far as is known, the deposition of sodium biurate has nothing whatever to do with any of them. In spite of the physical involvement of the joints, many gout patients live to a very old age.

Figures for the *mortality* from the disease are quite lacking. It is, however, probable that far fewer gout patients die than is the case in proportion with those afflicted with any of the other chronic diseases of this age, such as obesity, nephritis, or diabetes.

As to *function*, it can readily be imagined that the deposition of sodium biurate in the tissues of the joints will lead to an impairment of the movements of that joint. It is, however, remarkable how little impairment in the mobility of the joint is caused, when one considers the great disadvantage that the sufferer from arthritis of an infective nature undergoes. The damage to the joints from the infectious process is very much more pronounced. The tissues in the immediate neighborhood are stiffened, the muscles are atrophied, and the whole joint is often quite incapable of movement. In gout, the reverse is the case. In spite of the deposition of urate, the individual is able to move quite well, and in the intervals he may have no pain at all, either when quiet or when the joint is in active motion. Naturally, in very advanced cases, when there are enormous tophi present, these may interfere with movement mechanically, as well as hindering the functions of the various tendons and joint structures. Reference is made in some historical treatises to sufferers who competed in athletic games during the intervals between attacks.

**Pathology** (*Morbid Anatomy and Functional Pathology*).—The essential anatomical changes in gout are due to the deposition of sodium biurate in the various parts of the body, especially in and about the



joints and the tendon sheaths, and to the inflammatory or degenerative changes in these areas which immediately or remotely follow or precede the deposition of the urate. There is still no definite knowledge as to the reason for the deposition of the biurate of soda in the joint cartilages. According to Roberts, the biurates are deposited in the cartilaginous tissue, because the temperature here is lower than in any other part of the body, and the circulation less profuse, and because the cartilages are bathed by synovial fluid which contains a high percentage of sodium salts. The amount of sodium compounds is found to be highest in the cartilages, and next highest in the synovial fluid, throughout all the tissues in the body, according to the older writers. The presence of such large amounts of sodium salts, together with the lack of easy communication between the synovial cavities and the general circulation, and the lower temperature, were thought to account for the fact that the biurate was so frequently found deposited in the articulations. At death the whole joint is sometimes found to be affected. The articular cartilages are covered with patches, streaks, or points, of a white chalky material, which on analysis is found to be composed mainly of sodium biurate, with the addition of a small amount of calcium biurate. This substance is, in some cases, confined to the articular cartilages; in other cases it extends all through the structures of the joints, ligaments, tendons, synovial membranes, and the fascias of the muscles attached to the joints. In severe cases the synovial fluid of the joints is found to be filled up with masses of biurate. In very severe cases of long standing, the deposition may infiltrate the peri-articular structures and the skin, penetrating towards the surface and forming tophi that may even develop into ulceration. The synovial fluid is generally found to be thickened and reduced in amount; in the case of the large joints, such as the knee, there may be considerable effusion of fluid into the cavity of the articulation. In chronic cases the capsular tissues are much thickened. Should the individual die during an acute attack, it is common to find that there is an excess of fluid in the joints, even in the small joints of the foot bones, and that there are the classical signs of inflammation, redness, and edema.

Bass and Herzberg<sup>11</sup> have recently described cases wherein they had examined the content of the synovial fluid and of the blood in cases of gout. They found in two instances that there was about twice as much uric acid in the joint affected as was to be found in the blood of the same patient. This would seem to indicate that the joint had a peculiar power of selecting urates from the blood stream. They do not make any mention of having examined the other tissues of these patients.

It is possible to find other changes in old gouty joints, but these are not nearly so often observed in this age, when all classes of the population have access to medical advice, as was the case in former years. There may be erosion of the articular surfaces, and thickening, or hypertrophy of the ends of the bones. This change may be due to an associated infective condition, or the affection of the joints may have preceded the attacks of gout.

On closer examination, particularly with a low power microscope, one discovers that the deposition of biurate of soda is not upon the cartilage, but under the surface of it. If a thin vertical section is cut through the cartilage at the side of the deposit, it is found that the urate infiltrates through the matrix of the cartilage, beneath the free surface, and that it is composed of felted masses of pointed crystals. The deposit penetrates only to a small depth, rarely more than one-third or one-half of the entire thickness of the cartilage. It is further seen that this deposition ends directly under the articular surface, and as one proceeds from the articular surface, the deposition becomes thinner and thinner. Nearest the bone there is no deposition of sodium biurate. Where the deposition is smallest in amount, the pointed character of the crystals is most easily observed. Because of this fact it is held that the deposition occurs from the synovial fluid.

There has always been a great deal of discussion as to the essential cause of the biurate deposition. We know now no more than did the physicians of twenty-five or thirty years ago. Ebstein insisted that there is always a primary tissue necrosis. If this view be correct, it seems more likely that the areas of necrosis result from the toxic action of some unknown poison than from biurate infiltration. These necrotic areas are most liable to occur in the joint cartilages and in other cartilaginous and articular structures in which the normal lymphatic currents are slow. On the other hand, the sections of cartilage may be soaked in warm distilled water and the white chalky material dissolved out, after which one finds that the cartilage has resumed its normal appearance. Bradford Rose bases upon this his assumption that the necrosis is secondary, and due to pressure rather than to a primary change. At best, the erosion is only found where there has been a very slight deposition of the crystals.

Sir A. Garrod gave a capital description of the relationship between biurate deposit and gouty inflammation of the joint. After an extended series of observations of the joints of gouty persons whose previous history had been carefully ascertained, he concluded that those joints which had passed through an attack of gouty inflammation at some previous period always displayed the deposition at autopsy. Those joints which had not been so attacked were quite free from such depositions. On these premises Garrod formulated the proposition that "gouty inflammation is invariably attended with deposition of sodium biurate." It is probable that this idea is true, but it does not appear to be universally true that a joint which at some previous period of life has undergone an attack of gouty inflammation will invariably be found after death to exhibit these deposits. It is quite possible that there may be a reabsorption of the material by the blood and lymphatic stream, and so a complete return to normal on the part of the joint. The relative frequency with which the joints are affected with deposits corresponds closely with the frequency with which they are subjected to gout, as observed clinically. This conclusion is based upon the record of eighty autopsies on gouty subjects made by Norman Moore.

The most commonly affected joints are the metatarsophalangeal joints of the great toes; and not infrequently these are the only ones affected. The insteps, ankles, knees, hands and wrists are next in order; the elbows and shoulders are more rarely affected. The deposit may be present in nearly all the joints of the lower extremity, and yet absent from those of the upper. The deposition in the ear cartilage is exactly the same as that in the articular. The difference to the casual observer is that the ear is infiltrated from two sides, and in this case the cartilage is very thin. Tophi, however, rarely bulge out on both sides of the cartilage.

**CIRCULATORY SYSTEM.**—(a) *Heart.*—Hypertrophy and dilatation of the left ventricle are very frequently found, due, it is believed, to high tension and nephritis, against which the organ must work.

The aorta is generally thickened and atheromatous. The orifices of the coronary arteries are very frequently occluded by the atheromatous process, and this leads to degeneration of the coronary arteries, and consequently to malnutrition of the ventricular wall. There may be definite evidences from a pathological standpoint of angina pectoris due to this process. Fatty degeneration of the heart muscle is common for the same reason. Occasionally pericarditis is described as arising from gout; it is more probably due to an infection grafted on tissues, the resistance of which is lessened by gouty or nephritic processes.

(b) *Arteries.*—The arteries are almost invariably found sclerosed. It is not known at present whether the process is due to the gout or to the associated nephritis.

**RESPIRATORY SYSTEM.**—Occasionally deposits are found in the laryngeal cord. The lungs may exhibit signs of chronic bronchitis. Emphysema is very common.

**GENITO-URINARY SYSTEM.**—*The Kidneys.*—It has long been recognized that there was an intimate relationship between gout and nephritis. The form of the kidney involvement, which is found especially associated with gout, was that known as granular degeneration. Ebstein divided the kidneys into two classes: the one in which gout was the primary cause of the kidney disease, and the other in which the kidney disease anteceded the gout. Fitcher cites a case of the latter, in which a man aged twenty-four, who had had symptoms of chronic Bright's disease for many years, developed pain in the right toe. On autopsy, it was found that there were characteristic depositions of sodium biurate in the affected joints, confined to the articular cartilages. The kidneys were much contracted. Occasionally the autopsy on subjects affected with granular contracting kidneys discloses the existence of unsuspected biurate deposits in joints where the clinical history had indicated no antecedent inflammation. It may be generally claimed, says Bradford Rose, that the coincidence of articular gout with renal disease is more common among the poor and in-hospital patients than among those in better circumstances. In cases of lead poisoning, gouty implication of the kidneys is almost, if not quite, invariable. In private practice, on the other hand, and among the better class of patients financially, it is

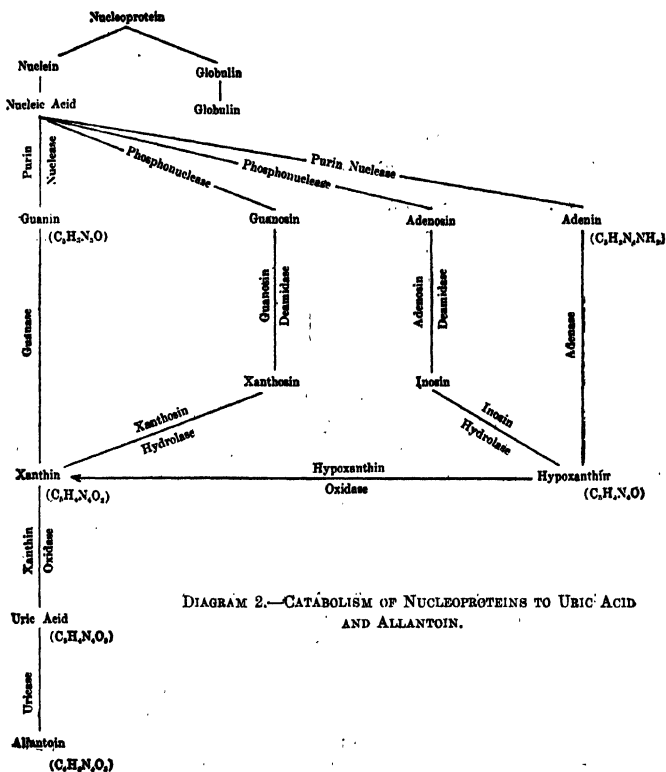
common to see articular gout, even of a chronic and inveterate character, run its entire course without any accompanying signs of structural disease of the kidneys. In addition to the granular secondary contracted kidney, one may meet the arterial sclerotic type. In these cases it is large, beefy red, and very hard. On section, deposits of sodium biurate are found. In the cicatricial substance the deposit is scanty, and occurs in specks scattered irregularly through the tissues. It is most frequently seen, and most abundantly met with in the pyramids, occurring in streaks running in the direction of the tubules, particularly towards the apices of the pyramid. The deposit is generally in the intertubular tissue, but it may also be found in the lumina of the tubules. Deposits are not so frequently found as was first believed. Norman Moore found them in only twelve of his series of eighty cases. Osler holds that the deposits must not always be interpreted as meaning gout, because they are found in individuals who have had no acute manifestations of the disease in life, and whose joints are found to be unaffected at autopsy. Bradford Rose draws attention to the fact that this deposit of biurate may be considered as outside the body, and so not gouty at all. It occurs upon tissue that is developed from the ectoderm, whereas the typical infiltration of biurate of soda, in gout, occurs in entodermal, or mesodermal tissue. While the older writers, both clinicians and pathologists, described a gouty form of kidney and attributed many of the signs found to this condition, the later studies of kidney pathology have failed to differentiate any particular form of renal disease associated with gout. These recent students, prominent among whom have been Volhard and Fahr, Christian and Mosenthal, have been more interested in the correlation of the clinical aspect with the pathological in their studies of the manner in which the kidney performs its vital work. That is to say, they have studied its functional activity and have failed to differentiate any type of renal change particularly associated with gout. Not only the gross appearance, but the microscopical changes are merely those of chronic nephritis, and to that section the reader is referred for further information concerning the kidneys.

**Physiology: Uric Acid Metabolism.**—The mass of information, and the number of papers published on purin metabolism, are so large, says von Furth,<sup>12</sup> that no one can claim to be familiar with all the details. The honest man can only pretend to give a survey of the situation as it is understood at present. As much of this work deals with hypotheses, statements that have one signification for one observer may be capable of quite a different interpretation by another. In a system like the present, one can only outline what one gathers from reading the voluminous literature dealing with the oxidation of purin.

**URIC ACID.**—It is necessary that we should first of all devote some attention to the subject of uric acid, for it is the substance with which physiologists and physicians of the last twenty years have been primarily concerned in studying the metabolism of gout. The later trend of opinion, however, has been to the effect that uric acid and its source do not play the principal part in the disease.



of formation of these substances are possible. If the purin bodies, or uric acid, are developed from the tissues of the metabolic subject, they are said to be *endogenous* purins or uric acid. If they have been derived from the cells of his food, they are said to be *exogenous* purins or uric acid. No matter what their source, nucleic acids are fairly similar in composition. They consist of four nucleotids, each of which contains



phosphoric acid, bases (either pyrimidin or amino-purin), and a carbohydrate hexose or a pentose. As far as known, all the steps in the digestion of the nuclein compound, from nucleic acid right down to uric acid, and in the lower mammals to allantoin, are caused by the action of tissue ferments. These ferments have been the object of much study in recent times. They are not universally distributed in all animals, nor are they to be found in all the tissues of any one animal. The catabolism of the nucleoproteins to uric acid and allantoin appears a very compli-

cated affair, but it really consists of a series of steps easily carried out experimentally with test tubes. The first step in the digestion of nucleoprotein is breaking it up into nucleic acid and protein (Diagram No. 2). On destruction of the nucleic acid, each nucleotid yields: (1) Phosphoric acid. (2) Two purin bases, guanin and adenin. (3) Two pyrimidin bases. (4) A carbohydrate group, hexose or pentose. Our interest in this digestion is confined to guanin and adenin, found in nucleic acid, for these two bodies belong to the purin series. The next step consists of deamination. This is a process whereby the amino or  $\text{NH}_2$  group is split off. It is probable, however, says Jones,<sup>13</sup> that deaminization may precede the splitting off of the group from the acid. In this process of deamination, adenin is changed to hypoxanthin, and guanin to xanthin, by their respective ferments. The next stage is an oxidative process, whereby hypoxanthin is changed to xanthin, and the xanthin, whether it comes from adenin through hypoxanthin, or from guanin direct, is converted by further oxidation to uric acid. Finally, in lower animals, uric acid is further oxidized to allantoin by a ferment known as uricase.

To Brugsch and Schittenhelm in Germany, and particularly to Jones<sup>13</sup> and his associates in the United States, is due the credit for not only having discovered several of these ferments, but also for having described their distribution in the various tissues of animals. The final enzyme, xanthin oxidase, is found in man, for example, only in the liver, and uricase, which further oxidizes uric acid to allantoin in the majority of mammals, except man and the anthropoid apes, is not to be found in the tissues of man at all. Consequently it is believed that in man uric acid is the final product of purin digestion. While the possibility of synthesis of uric acid in the body must be kept in mind, it is probable, according to the best authorities, that the uric acid excreted by man, in the urine, all comes from purin metabolism.

The study of these ferments in the various tissues, although difficult, has yielded very interesting results, principally at the hands of Jones and his pupils. Dog's liver, for example, contains guanase that deaminizes guanin to adenin, but not adenase, which changes adenin to hypoxanthin. In human beings, adenase is not present in any of the organs; guanase is present in the kidneys, liver and lungs, but not in the spleen or pancreas. Consequently, the theory advanced is that guanin can be deaminized to xanthin in any of the organs where the ferment is found, but not in others, and that adenin is not changed in the human being at all. If the adenin fraction is split off, it must be changed in some other manner other than by deamination in this way.

The ferment xanthin oxidase that oxidizes hypoxanthin and xanthin to uric acid is entirely independent of the deaminization described above. In human beings, this ferment is found in only one organ, the liver. Apparently, therefore, the liver is the site of manufacture of all uric acid in human beings. It seems that this must be the case, because it is the only organ in which hypoxanthin can be oxidized to xanthin, and similarly xanthin to uric acid. In other animals than

man, xanthin oxidase may be present in other organs besides the liver. For example, it is found freely in the spleen of the ox.

While the major portion of the biochemist's attention in connection with purin metabolism has been directed toward the breaking down of the nucleic acid molecule in the body, it must be borne in mind that not all uric acid excreted by an individual comes from his own tissues, but some of it from the cells of the food digested. Again, it is highly probable, although so far we are without any proof of the hypothesis, that a good deal of the ingested purin bodies giving rise to exogenous purin are changed in the intestinal tract or mucosa. We are reasonably sure that the adult animal has the power to synthesize his nucleic acid-containing material, because in the eggs of birds and insects, nucleo-proteins are absent, and yet, in the development of these eggs to the adult form, nucleo-proteins are formed in large amounts. This process of synthesis of nucleic acid-containing tissues from simpler forms must certainly take place in the fetus *in utero*. The salmon, when it goes up the river to spawn, does not take any food, and yet it forms nucleo-proteins. Then again in man, if the individual is fed on milk and eggs, and other purin-free diets for a long time, he does not lose either in his cellular activities or in his cellular content. Yet we must be reasonably sure that whenever an individual lives, the protoplasm of the cell suffers, and the nucleus must be in a constant state of wear and repair. This repair can only be accomplished if the nucleo-proteins are available. Again, it is possible to change the uric acid content of the urine by various processes that are compatible with life. An individual standing in a state of rigid muscular contraction, or a patient immediately after delivery, displays a remarkable change in the amount of uric acid excreted. The individual diet has not been changed. The expression of the subject's metabolic activity is different. Uric acid metabolism should not, says von Furth, be looked upon as the expression of one part of the body activity alone. The uric acid metabolism may be changed, for example, by exaggeration of glandular activity following the use of pilocarpin, by increase or destruction of the tissues by x-rays, and by pathological processes like phosphorous poisoning, atrophy of the liver, cirrhosis, jaundice, leukemia, fever, and pneumonia. All of these factors increase the endogenous purin. In view of these facts it is, of course, unreasonable to suppose that all the activity of the change in metabolism of these bodies, in so widely distributed processes as those mentioned above, is centered in one organ. Consequently, the production of uric acid is to be looked upon as a general body function, and when one considers the endogenous purin metabolism, one must look upon it as an expression of the general wear and tear of the body.

The amount of uric acid in the urine varies in individuals. As a rule, each individual has a fairly uniform level of his own, and the level varies only when one tests a large number of individuals. The amount ranges from 0.4 gram, upon a purin-free diet, to 1.0 gram upon a mixed diet. The amount of uric acid appearing in the urine depends upon: (1) the amount of purin bodies taken in the food, that is to say,



the amount of exogenous purin; (2) the degree of destruction of tissue nucleo-proteids; (3) the amount of purins free in muscle tissue; (4) the degree of conversion of purins into uric acid; and (5) the retention of uric acid by the blood and tissues, together with the ability of the kidneys to excrete uric acid. A small amount may be formed from the synthesis already alluded to, but for practical considerations of the problems of uric acid production in health and disease, the amount so formed is negligible.

It is apparent that the main way in which the amount of nucleic acid, or purin products available in the body may be subjected to change, is by means of the food. The amount may be increased greatly by giving the individual a diet rich in nucleic acids. The edibles containing large amounts of nucleic acids will be those that are cellular in structure rather than extracellular, and the classical examples are liver, sweetbreads, and kidneys, beans and peas, in contradistinction to milk, eggs, bread, fats, and other meats and vegetables. It was supposed that coffee gave rise to an increased amount of uric acid, but it now seems probable that methyl purins do not appear in the urine as uric acid. Eating large amounts of meat, even if it is not from the organs mentioned above, will also raise the purin intake, because of the free purin products contained in the muscle tissue. Taylor and Rose<sup>14</sup> found that a diet rich in protein but free from purin will raise the uric acid content of the urine. But in health the amount of the urates in the blood is not raised as high as one would imagine, because the tissues take up the surplus, and a larger amount is excreted in the urine. Normally, from 1.5 to 2.5 mg. of uric acid per 100 c.c. of blood are to be found, but McClure and Pratt claim that the amount might be raised to 3 mg., and the individual still be considered as normal. Fine found that in health the tissues contained an amount comparable to that found in the blood.

**URIC ACID METABOLISM IN DISEASES OTHER THAN GOUT.**—Leathes, Kennaway, and Cathcart<sup>15</sup> have shown that the increase of uric acid output in the urine, in individuals suffering from fever of any kind, is due to the muscular processes in the body, resulting in an increase of heat production. The uric acid increase in the urine does not come from increased voluntary muscular work.

In the blood, there are numerous instances when the amount may be raised greatly. In the early stages of nephritis it may range from 4 to 8 mg. per 100 c.c.; in the later stages, particularly in uremia, the amount may be as high as 20 mg. per 100 c.c., without the individual suffering any of the signs or symptoms of the so-called irregular gout. Also, when a lobar pneumonia is resolving, with the enormous destruction of polymorphonuclear leukocytes that then takes place, or, in a similar instance, where a myeloid leukemia is treated with benzol or the Roentgen-ray, there must be a high content of uric acid in the blood.

**URIC ACID IN NORMAL BLOOD.**—The blood normally contains uric acid. In health, and on a purin-free diet, the quantity does not exceed from 1 to 3 mg. of uric acid per 100 c.c. of blood. For a discussion of the older ideas of the manner or the form in which uric acid circulated in

the blood, the reader is referred to the historical section. At present it is believed that it circulates as biurate of soda, or monosodium urate. Gudzent<sup>16</sup> has shown that this salt may occur in two isomeric forms (see Diagram No. 1). The first is the laktam form, which is unstable but soluble in blood-serum of about 18 mgm. per 100 c.c. From this form, it passes into the lactim form which is only soluble to the extent of 8 mgm. per 100 c.c. This difference of solubility has been used by Gudzent to explain the deposition of urates in the tissues.

URIC ACID IN GOUT.—Over twenty years ago, von Noorden<sup>16</sup> said: "It is not very alluring to-day to write anything regarding the theory of gout in a book that is essentially devoted to the presentation of facts. All the theories advanced up to the present time have fared very badly. Part of the material is much too insufficient and much too ambiguous." After over twenty years this opinion is sustained. While a great number of papers have appeared, dealing with the chemical and clinical aspects of the disease, they have tended to obscure the old views without giving us any new ones in which we may put much confidence. In fact, we have now almost accepted the belief that uric acid, or rather the monosodium salt found in the blood and through the tissues, is incidental rather than the cause of the disease, just as the urinary sugar has assumed a relatively less important place in diabetes.

The excretion of uric acid in the urine of patients suffering from acute gout, when on a normal diet, does not differ greatly from that of the normal individual on the same diet. It tends to assume the lower level on the normal. For a period of from one to three days before the onset of an attack of acute gout, the elimination of uric acid is greatly reduced. Soon after the onset of the acute attack, however, the amount of uric acid excreted rises rapidly, and for a few days remains well above the average, and then subsides to the old level of normal, or even lower than before the attack. In the intervals between attacks the elimination of uric acid remains within the normal limit. Of the two changes from the normal level, the increased excretion during the attack seems to be more usually observed than the diminished excretion before the attack comes on. It is noteworthy that certain cases of rheumatoid arthritis, or osteo-arthritis, have been observed to show uric acid curves similar to that found in gout.

When the disease becomes chronic, the excretion of uric acid, if patients are kept on a definite diet, remains at about the lower limit of normal for a series of healthy individuals on the same diet. There may be even slight retention. If the gouty persons are put upon a purin-free diet, it is thought that they excrete less endogenous uric acid than normal people, and it was thought that when given purins in the food, the rate of excretion of these exogenous purins was slower than normal. The recent studies of Pratt and McClure make it probable that such a slowing up of the process of excretion of the purins added to a standardized diet is not by any means confined to gout. Even on a purin-free diet, the blood of the gouty patient contains an excess of uric acid, there being from 4 to 9 or even more milligrams of uric acid per 100 c.c. of

blood. This increase in the amount of uric acid is found whether or not there is an acute attack at the time. It is also found whether there is a marked or a hardly noticeable alteration in the functional activity of the kidneys. As far as is known, there is no relationship between the amount of uric acid in the blood, and the occurrence or severity of the attacks (Pratt and McClure, and Bass and Herzberg).

Gudzent,<sup>18</sup> working with the old methods of uric acid estimation in the blood (titration with permanganate of potash, or precipitation and weighing), found that the blood in gout contained about as much, or more, monosodium urate as it would hold in solution, that is to say, 8.03 mg. per 100 c.c. of blood. He thought that there was always a highly saturated solution of urates bathing the tissues. All the recent works produced in the United States since the publication of the last system of medicine (Futcher's<sup>1</sup> article on gout in Osler and McCrae, 1914) have been based on observations made with the new methods of colorimetric estimations of uric acid in blood, urine, and tissues. These methods have been brilliantly developed by Folin and his associates in the last six years. By the aid of these methods (all others are now discarded), it has been found that the gouty individual has, on a purin-free diet, and independent of any attacks, the amount mentioned above—that is to say, about from 4 to 9 mg. of uric acid per 100 c.c. It is probable also that this uric acid circulates in the blood as sodium biurate and is not found in any complex salt form, as was judged to be the case by the earlier authorities. McClure and Pratt found that the blood of the vast majority of normal people contained less than 3 mg. of uric acid per 100 c.c., whereas in all the cases of gout that they examined the blood-content was more than 3 mg. If the increase above 3 mg. was accompanied by the presence of less than 50 mg. of non-protein nitrogen, that is to say, if the patient were not suffering from the retention products of protein metabolism commonly due to nephritis, the probability was even greater that the patient had gout.

It has long been known that the gouty have been subject to interstitial nephritis, but it was only with the introduction of these newer methods for ascertaining the functions of the kidneys that one realized how early in gout the kidneys are apt to be affected. The physician knows that he is able to get a far better idea of the condition of his patient at the present time, and to make a far better prognosis, than was the case before their introduction. "Reasons drawn from the urine pot are as brittle as the vessel containing them" is not nearly so true now as in Bright's time, and even less true, if one adds to the information derived from the study of the urine, the information that one can draw from studies of the blood by the methods developed in recent years.

McClure and Pratt found in their series of gouty patients, judged by the standards of functional tests, that there was reason to believe that serious damage to the kidneys existed, even when on the old basis of judgment the patients were believed to be free from nephritis. They found that the phenolsulphonephthalein excretion was much lower, the specific gravity of urine fixed, the amount passed at night much increased,

and in all cases that there was retention of the non-protein constituents in the blood.

They then injected uric acid intravenously, in normal and in gouty persons, and found that the excretion varied greatly, both in time and in amount, that the uric acid excretion might start in a few hours, or might be delayed over several days, and that even the amount recovered might be a small fraction of that introduced intravenously. Again, in the case both of the normal and of the gouty person, the amounts to be found in the blood varied greatly after the intravenous introduction of the acid. In the case of four out of five non-gouty patients, however, the increase of excretion of uric acid lasted less than forty-eight hours, whereas with three out of four patients suffering from gout, it lasted longer than forty-eight hours. The physicians decided, therefore, that the exogenous acid was held longer in the blood stream of the gouty than was the case with the non-gouty patients. Again, a larger proportion of the exogenous uric acid, introduced into the circulatory system by intravenous injection, disappeared completely in the gouty person than in the non-gouty. There was no way at all of accounting for this diminution in the amount of uric acid. It was not to be found in the urine, and had vanished from the blood. No acute attack followed its introduction. In two or three instances the amount of non-protein nitrogen of the blood was increased. (This increase was even greater, proportionately, than was the uric acid increase following the intravenous administration of uric acid, or the feeding of sweetbreads to the patient.)

After feeding patients who were on a purin-free diet a definite amount of sweetbreads, which are of course very rich in nucleic acids, it was found that the exogenous output of uric acid was completed just as fast in the gouty as in the non-gouty cases. There was, furthermore, a marked variation not only in the time, but also in the amount of exogenous acid so excreted. Consequently, the amount, as well as the time, of uric acid output from a purin meal varies greatly. This variation is so great, in the case of healthy or of non-gouty individuals, that it is impossible to attribute to it any of the evils that result in gout, even if the variation in gout be greater.

**Theories of Gout.**—Garrod, as far back as 1848, thought that possibly the whole cause of gout might be selective renal retention of uric acid. Since then, the number of theories advanced as to the causation of the disease has been large, and they are probably accompanied by more controversy, with less actual result, than any other subject. It is impossible to discuss here either the various theories or the arguments supporting or depreciating their stand. The reader must be referred to one of the larger books on gout, or on purin metabolism, for a full description of the subject.

As for facts, we know that gout is a disease in which, in life and after death, deposits of sodium biurate are found in many of the joints, particularly in the cartilages and periarticular structures. It is also characterized by a diminution in the functional activity of the kidneys, this diminution being better shown by the functional test than by the

old changes that formerly suggested nephritis to the practitioner. We are almost tempted to say that the known facts at our disposal are the chronic interstitial nephritis characterized by a selective retention of uric acid. It is this typical retention of uric acid that after all distinguishes the early stages of gout from nephritis that is not gouty in character, and that is not accompanied by the deposition of biurate in the joints. But so far we have no definite information either as to the cause of the change in uric acid metabolism during the paroxysms of acute gout, or as to the cause for these paroxysms occurring at all. In view of the fact that the same substance is found in the blood in excessive amounts in this disease that is also found in the lesions where the individual experiences discomfort, it is supposed that there occurs for some, as yet unknown, reason a precipitation or anchoring of this substance, sodium biurate, in the tissues, which is associated with the pain and swelling. We are not by any means sure that it is the deposition of urates that causes the attacks. Indeed, as uric acid retention precedes the attack rather than accompanies it, it seems probable that the absorption of the urate from the blood, rather than the deposition in the joint, is responsible for the local pain, swelling, redness, and immobility of the joint. It may be possible that during the period of retention the uric acid is held in the blood, changed into some form that cannot be excreted by the kidney, and that the deposition in the joint, in an absorbable form, occurs simultaneously with the attack. Again, the pain is still severe in the joint, while there is a great outpouring of urates through the kidneys. As Magnus Levy says, the inflammatory process extends far beyond the margin of the joint containing the urates, far farther than could be accounted for by the mechanical effect of the deposition, even if it were a much more irritating substance than it is.

From the standpoint of biochemistry, the actual cause of gout is the failure of the human organisms to destroy uric acid to a more easily excreted product like allantoin, in the same way that the lower mammals do. But we should be ill-advised to consider gout a disturbance in the ferment activity. First of all, we realize that the ferments have not yet been studied completely. Then, not only is the purin metabolism seriously disturbed, but there are evidences of nitrogenous retention. Possibly some of the retained nitrogenous bodies may be synthesized in the gouty, to uric acid, and the uric acid so procured infiltrated in the tissues. On the other hand, this retention, or subsequent loss of nitrogen in the body, is not accompanied by any change in weight.

We do not fully understand the metabolism of purin, nor of nitrogenous bodies in gout, or even whether or not the acute painful attacks or anatomical changes in the heart, kidneys, and blood-vessels are caused by urate retention. Indeed, Daniels and McCrudden<sup>17</sup> have shown that it is possible for typical attacks of gout to occur when the individual has a low uric acid content of the blood, either without medical intervention or following the administration of atophan. In the administration of atophan, there have been instances when the patient's blood uric acid was away below normal, and yet attacks occurred. Conversely,

Bass and Herzberg showed that uric acid could be injected into the blood of gouty patients until the content was as high as 10 mg. per 100 c.c. without any of the symptoms coming on.

Bass and Herzberg also showed that the intravenous injection of uric acid caused less high concentrations, less high contents of urate in the blood, than when the procedure was carried out on the non-gouty. From this experiment they deduced that the tissues took up the urate selectively, that is to say, that more was taken up by tissues that already had a tendency to be gouty.

One point that causes one to doubt that selective uric acid retention and nephritis are the causative factors of gout, is that no authority has ever shown that there is higher uric acid retention when the evidences of nephritis are more marked than in other cases, also undoubtedly gout, or that there is more marked evidence of kidney impairment at the time of the attack than when the sufferer is free from symptoms. Again there are no studies of the renal functional activity in the not rare cases where the individual has gout and yet has never experienced an acute attack.

In the urine, it is fairly well known that the salt and uric acid itself are kept in solution by phosphates, but no one knows the mechanism by which uric acid is kept in solution in the blood stream. Yet about four or five times that normally found, or twice that found in the most severe cases of gout, are quite commonly met with in the blood of people suffering from nephritis, especially in uremia. Howland's<sup>18</sup> work on phosphate retention would almost lead one to believe that the retention of large amounts of phosphate by the nephritic kidney was responsible for the increased amounts of sodium urate held in the blood stream in nephritis, without there being any tendency to precipitate it out into the joints, or connective tissues, as happens so uniformly in gout.

**Historical Summary.**—Hippocrates, who lived about 350 B. C., showed in his writings that he was familiar with the symptoms of gout. Aretaeus, who wrote about the middle of the second century A. D., described the disease, and gave it a name that has lived to the present—podagra. He classified the disease as to the part affected: podagra of the foot, gonagra of the knee, and chiragra of the hand. He it was who described the athlete suffering from gout who won in the Olympic games between two acute attacks. It is likely that the earlier writers noticed the hereditary tendency of the disease. About the thirteenth century, the word gout (from gutta, a drop) was introduced, and it owed its introduction to the prevailing belief that the disease was due to the presence in the blood of some abnormal element which was thrown out or discharged into the joints, drop by drop, with each successive acute attack. It is, however, to the master of English medicine, Thomas Sydenham, who lived from 1624 to 1689, that we owe our best description of the disease from the older writers. He himself was a sufferer from the disease. One of his sayings that has lasted, is that: "More wise men than fools are sufferers from the disease."

Wollaston, in 1797, discovered that the concretions contained uric

acid. In 1776, Scheele and Bergmann discovered that uric acid was to be found in vesical calculi, and in the human urine. After the discovery of Wollaston, there was little progress in the study of the disease until Garrod, in 1848, found that the blood and interstitial tissues of gouty persons were surcharged with the same compound; that is to say, with uric acid. From that day until the discovery of Brugsch and Schittenhelm, in Germany, and Jones and his associates in the United States, the opinion was held by most authorities that the uric acid deposition in the joints was the actual cause of the disease. Dating from these later writers, there has been a steadily growing conviction that uric acid plays little or no part in the actual causation of gout. Although it is well known that uric acid plays by far the greatest rôle among the abnormal constituents of the diseased joints, and is supposed to be actually collectively retained by the kidneys in this disease, it is felt at the present time that the uric acid is merely an incidental, just as we now have relegated to a subsidiary place the finding of sugar in the urine of diabetics. The uric acid in gout is probably a weapon, and not the actual cause of the disease.

Following Garrod, the British physicians of the nineteenth century did a great deal to develop many ideas of gout, particularly from its pathological standpoint. Many of these conceptions, unfortunately, have been proven erroneous, but that does not detract from the zeal with which the physicians attacked a problem that even now is accompanied by tremendous difficulties.

Garrod was the first to claim that there was a diminished excretion of uric acid in gout, and he believed that this was true of the acute as well as of the chronic form of the disease. From then until the time of Sir William Roberts there was little progress made. He was the one to develop the theory that the uric acid circulated in the blood, in the form of quadriurate, and that its deposition was dependent upon the high sodium salt content of various tissues, and the absence of free communication between these tissues and the general systematic circulation. The synovial sacks, for example, were shut to more free blood circulation. Undoubtedly, part of his contention has been upheld clearly, that the cartilages and synovial fluid are higher in sodium salt content than any other parts of the body, but it has been definitely established that there is no such thing as the quadriurate.

Burian, in 1905, demonstrated the fact that the muscle purins, particularly the hypoxanthin, were the main sources of the endogenous fraction of uric acid. He found that muscular exertion is always accompanied by a decided rise in the output of uric acid, and that the individual has a fairly constant range of daily excretion of uric acid.

Other experiments of that period were devoted mainly to the attempt to prove the location of formation of uric acid.

Ebstein held that the local manifestations of gout were due to nutritional changes, resulting in necrosis, that was later followed by infiltration with the sodium urate crystals. He was uncertain as to the cause of this necrosis, but thought it was primarily due to a special ferment.

Then Kolesh and Crofton have produced arterial and renal lesions on the injection of hypoxanthin into animals. This has been brought forward to support Brugsch's and Schittenhelm's hypothesis that the disease was due to ferment abnormality. Brugsch and Schittenhelm, and Jones, were the principal students to develop the knowledge of ferments involved in the process of purin metabolism, but the two German investigators were in error in that they held that gout was due to the absence of a uricolytic uricase, which they claimed was normally present in the liver, and the function of which was to convert uric acid into allantoin. There seems every reason to believe that at no time is uric acid split further down. Minkowski offered an explanation that the uric acid entered into some mysterious chemical combination in the blood, which prevented its excretion by the kidneys. As it is normally excreted by the kidneys in health, and as its amount can be definitely ascertained by Folin's method, even when it is added quantitatively to blood in a test tube, and as an increase is shown on intravenous administration, it seems hardly likely that it would enter into any unrecognizable combination.

Umber has been a prominent supporter of the theory that renal inefficiency, and the affinity of the tissues for uric acid, is the probable cause of the disease. He claims that if the idea of selective retention in the tissues be repudiated, it would be difficult to understand why gouty patients do not simply expel all the compensatory hyperexcretion of uric acid, just as is found in leukemia and in pneumonia. In the gouty individual there must exist some cause which makes a compensatory uric acid excretion impossible, and that is possibly a retention affinity of the tissues.

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## CHAPTER II

### OBESITY

BY WILLIAM FLETCHER MCPHEDRAN, B.A., M.B.

Definition, p. 39—Etiology, p. 39—Symptomatology, p. 39—Physical findings, p. 40—Special examinations, p. 41—Functional tests, p. 41—Fröhlich's syndrome, p. 41—Diagnosis, p. 41—Complications, p. 42—Association with other diseases, p. 42—Treatment, p. 42—Prophylaxis, p. 42—General management, p. 42—Diet, p. 43—Treatment of symptoms, p. 47—Hydrotherapy: mechanotherapy, p. 47—Organotherapy, p. 48—Exercise, p. 48—Medicinal treatment, p. 49—Prognosis, p. 49—Pathology, p. 49—Fat metabolism, p. 50—References, p. 51.

**Definition.**—Obesity may be a disorder of metabolism, characterized by an excessive amount of bodily fat, distributed over the whole body, but more marked where fatty tissue is normally present; or it may be an evidence of disturbance of the glands of internal secretion, and here the most commonly affected are the pituitary and thyroid glands.

**Etiology.**—PREDISPOSING CAUSES.—*Climate.*—Obesity is common in low-lying countries of the temperate and Arctic regions.

*Sex.*—Females are much more likely to become obese than males, because the percentage of hemoglobin in women is lower; consequently the oxidizing power is reduced, and the foods are more likely to be stored than burned. The more quiet life and the greater tendency to eat concentrated nourishment also predispose to obesity. In a large number of cases, the puerperium or menopause starts the increase of weight or accelerates the increase started before.

*Race.*—A race that eats easily oxidizable and highly prepared foods is more likely to get stout than one that has to manufacture its own foods from simpler food intakes. For example: the consumption of sugar in the United States has increased enormously in the last century. Whereas sugar was formerly manufactured from starch intake, the modern individual takes the carbohydrate—the main fuel of life—in a highly soluble, readily oxidizable sugar.

Obesity is common in races that are indolent, sluggish, and lead a luxurious life. The Orientals, Dutch, and certain African races tend to become obese.

*Heredity.*—Heredity plays a very important part in obesity.

**Symptomatology.**—The history of rapidly progressing increase in weight is rarely obtained from the patient. It may date from any time, but usually from the period of material success, in which the individual does not have to exert himself so greatly, physically or mentally.

Ebstein divided obesity into three stages: the enviable, or majestic, followed by the comical, and the last and most serious, the pitiable.

The symptoms at first are almost unnoticeable. The patient is able to do all his physical and mental work, possibly better than a corresponding individual of normal weight. Many have noticed the grace of men and women weighing in the neighborhood of two hundred pounds. However, the increase in weight, unless corrected, is apt to progress, and soon slight inconvenience, or shortness of breath on exertion, with possibly some edema of the ankles and feet in the late afternoon, are noticed by the patient. For years, no other disturbance may be experienced, but then marked severe dyspnea, due to the heart having to work so hard against the thick chest wall, against the increased pericardial fat, and against the poor descent of the diaphragm, as well as against the vast amount of tissue through which blood must be forced, may come into play.

**PHYSICAL FINDINGS.**—Most writers have divided the obesity due to errors of diet into two classes: the *plethoric* and the *anemic*. It is probable that many of the anemic cases were really due to glandular disease rather than to metabolic disturbances, and were unrecognized because of lack of investigation with the x-ray on the sella turcica, or through lack of performance of various functional tests.

**Plethoric Form.**—In the plethoric form the appetite is greater; the muscles are strong and voluminous; the complexion is highly colored; the skin is soft and at times appears congested; the neck and abdomen are particularly large; the perspiration is always free. Although the heart beat is strong, it is never seen or felt, because of the heavy chest wall. The pulse is slow and high in tension. The blood is more highly concentrated than normal. The red blood-cells may be as high as 7,000,000 and the hemoglobin up to 120 per cent. On palpation, the fat is felt to be firm and not at all edematous. At first, one finds the heart surprisingly small for the size of the body. Investigation should best be made by means of the x-ray, for it is always difficult to determine the outline by percussion.

Later in life the heart becomes irregular, and easily dilated. Signs of arterial disease, such as tortuous temporal artery, radial artery, or arcus senilis, become evident. At first, the heart sounds are clear, but, with the exhaustion of the myocardium, there is relaxation, and murmurs are evident.

As the circulation fails, the muscular power diminishes. Profuse sweatings occur, and at the same time one can find signs of embarrassment of the pulmonary circulation. There may also be evidences of passive congestion of the kidneys and the gastro-intestinal tract. There may be albuminuria with hyaline and finely granular casts, red blood-cells, and a much reduced volume of urine. Then, in the gastro-intestinal system, there may be alternately constipation and diarrhea. With the development of obesity, there is a marked tendency toward a diminution, in both sexes, of the primary and secondary sexual char-

acters—azospermia in the male, and amenorrhea in the female, are frequently found.

*Anemic Form.*—The anemic type of the disease is rarely as marked as the plethoric. Early in the increase in weight, the muscular exertion becomes difficult, because of the anemic state. The hemoglobin is greatly reduced; it may be as low as 30 per cent., and it is accompanied by an increase in the leukocytes, just as in secondary anemia. All the bodily surfaces are pale and generally somewhat edematous in the dependent portions. The perspiration is excessive, and owing to large areas of skin being in contact, irritation, or even eczema, are easily noticed.

As the anemia is such a prominent feature, the vigorous active circulation found in the plethoric type of the malady is not in evidence here. Poor circulation, characterized by enlargement of the heart, with murmurs and edema, are early found. The individual is often a poor eater, but even then specializes on carbohydrates without much residue.

*SPECIAL EXAMINATIONS.—Functional Tests.*—In a person who is over weight, an effort should be made to discover whether the obesity is due to error in diet or to a failure of activity of the thyroid or pituitary gland. The patient should be placed on a diet of 15 to 25 calories per kilogram of his calculated ideal weight. If the weight does not decrease on this diet, or if the loss does not continue more than a short time on this diet, one must take steps to ascertain whether the disease is not due to failure of one of the internal secretions; in this case the organ extracts of the hypophysis or the thyroid should be used.

Before utilizing the organic extracts, the investigator should have the sella turcica x-rayed and the carbohydrate tolerance tested, that is to say, the amount of the glucose that the individual can take on an empty stomach without exhibiting glycosuria. Normally, the individual would not be capable of assimilating 250 grams of glucose.

In addition, the visual fields should be examined, to make sure that any possible tumor of the hypophysis has not affected the optic tracts. In case of the overweight caused by thyroid insufficiency, it must be remembered that thyroid extract reduces not only these tumors, but also those due to other conditions.

*FRÖHLICH'S SYNDROME.*—While this trouble is primarily a disturbance of the function of the pituitary gland, the sufferer is led to consult the physician often on account of obesity, and it may well be considered here. Signs of pituitary abnormality may be discovered early in life. When fully developed, there is not only obesity, but sexual infantilism and retardation of the general growth. The fat is found on the trunk and buttocks; the hands and feet are small; the extremities are short and rounded; and there is a general feminine type of figure evident. There is a general retardation or regression of the primary and secondary sexual characters.

*Diagnosis.*—The diagnosis of obesity is not difficult. It must be remembered that obesity is a symptom and not a disease *sui generis*. Insurance companies have had sufficient experience with the expectation of life, to be certain that their ideal weight tables for various

heights and ages are founded upon statistics so generous that they must be right (indeed some authorities consider them too high); and the physician with a scale and sufficient interest to weigh all his patients can readily decide whether the patient is of good weight or not.

In reference to the ideal weight, Guthrie<sup>1</sup> has made use of the following formula: Ideal weight = 110 pounds +  $(5.5 \times \text{the number of inches taller than 5 feet})$ . Thus, if the height is 5 feet 10 inches, the ideal weight is  $110 + (5.5 \times 10) = 165$  lbs.

The disease most commonly mistaken for obesity is *myxedema*. Here one finds greater disturbance of the lines of the face, less dyspnea, and much more marked mental torpor than in obesity. The skin is harsh, dry, thick, and seems to confine fat that is thicker and harder than one finds in obesity. There is often tachycardia. But the administration of the thyroid extract in myxedema not only reduces the patient's weight, but tremendously improves his general physical and mental state, effecting the improvement more rapidly than in obesity.

*Dercum's disease (adiposis dolorosa)* is a rare condition. The symmetrically placed tumors of fat are tender. The masses are not uniform in size or shape, and there is no sweating.

Investigation should be made to differentiate the type due to hyperalimentation, from that due to glandular deficiencies. These have been discussed under the head of Functional Tests.

**Complications.**—The most serious complication is failure of the circulation due to insufficiency of the myocardium. It is fatal in a large number of patients. Occasionally, edema of the ankles may make movement impossible, and hence the heart muscle loses the little stimulus it has to increased exertion.

In the respiratory system, emphysema, with chronic bronchitis and myocardial degeneration, make the prognosis in pneumonia bad. Or the patient may have bronchopneumonia from chronic bronchitis.

In the digestive system, chronic constipation, with hemorrhoids, is often found.

**Association with Other Diseases.**—Obesity is often found with gout, diabetes mellitus, and heart disease.

**Treatment.**—**PROPHYLAXIS.**—Early in life, children showing a tendency to great overweight—particularly if their parents have had the same disposition—should have the fat-forming substances restricted in their food. They should metabolize their own sugar from starches, and take amounts so calculated that their weight increase will approximate normal limits. Physical exercises should be encouraged.

In adult life, those inclined to be stout—even if the weight is only five or ten pounds over the calculated ideal—should be advised to restrict their diet to keep the weight down to approximate the ideal closely. Outdoor exercises or physical training, particularly the use of a system of exercises which benefits the abdominal musculature, should be carried out regularly. The best of these exercises, to the writer's knowledge, are those found in Muller's "My System."

**GENERAL MANAGEMENT.**—If the patient is carefully instructed by

the physician, as the pediatrician instructs the mothers of his patients, the cure of obesity in the majority of cases will be simple. Indeed, the weight lost may be greater and more rapid than the physician desires. The patient should be warned early that rapid loss of weight is accompanied by grave dangers. Its acquisition has been the result of years of undesirable living, and it is unwise to expect a treatment to be completed in a few weeks. The plan of treatment is to reduce weight by the loss of the superfluous fat. Care must be taken not to destroy the body proteins by underfeeding, excessive exercises, or by the ill-advised use of drugs. In fact, as these patients are generally weak, it is desirable to set before them the idea that they should feel progressively stronger.

If the amount of weight to be lost is more than five or ten pounds, six to eight pounds per month is the highest rate of loss that should be encouraged. With the very obese, the total amount of weight lost should not be more than about fifty pounds per year. The patient should also be warned early that any departure from his routine, or any resumption of his old habits, after the cure is completed, will be followed by a rapid increase in weight again.

It is the aim of the treatment to render to patients more economical machines than they have been running, so as to use their food to advantage. They have either been eating too largely or eating the wrong foods, and undergoing too little bodily exertion.

The question will soon arise as to whether better results can be obtained at home or at a health resort where the cure of metabolic disorders is a *spécialité*. The patient who, for a limited time, goes to a health resort, lives under conditions that are unnatural; and little will be accomplished at that time by changing his way of life, for he will go back to the old routine easily. At the same time, the situation is somewhat analogous to the treatment of tuberculosis or of diabetes. At an institution, the patient is apt to see others in a worse condition than his own, and with others, is apt to develop, or to have fortified, those habits of mind that must govern his life after his return. If the patient will look on the institution as a type of school, it is to be recommended; otherwise, better results can be obtained by home treatment, provided the individual has the necessary backbone to obey instructions. Little can be accomplished if there is going to be interference on the part of relatives. The patient should have scales easily accessible, and be weighed every Sunday or Monday morning. The day should be specified to insure the regularity of the weighing.

DIET.—The patient who is slightly overweight can be reduced by confining his meals to meats, fish, chicken, green vegetables, and fruits (Barker).

All the diets are based on the same principle—to **diminish the caloric value of the diet** so far as is consistent with the maintenance of nutrition and strength. Not only are the quantities of foods reduced, but their character is so changed that the individual gets a diet that is voluminous rather than one that is concentrated.

While diet on a caloric basis is governed by the surface area of the body, in exact metabolic experiments, for clinical purposes, the individual can be well treated by computations based upon weight. For the person doing an average amount of work, 35 calories per kilogram (2.2 pounds) per day is all that is necessary. Means<sup>2</sup> has shown that basal metabolism in obesity is unchanged per unit of body surface. If there is a slight reduction, it is probable that the glands of internal secretion are disturbed. The diet should be reduced so that in place of getting 35 calories per kilogram (the physician can easily calculate the patient's weight of kilogram, by dividing her weight in pounds by 2.2) the diet should be three-fifths of the ideal amount. The plan is to give a smaller amount of energy than the body spends, so that to make up the deficit, the individual will draw upon the fat that has been stored, and burn it. It is probable that this process involves a removal of the fat from the general system to the liver, removal of hydrogen atoms by the liver, and then destruction of the fat into carbon dioxide and water.

It is important that the diet should contain an *adequate amount of nitrogen*. For Americans, there should be about 15 to 16 grams of nitrogen per day; that is to say, between 90 and 100 grams of protein. The first consideration is to provide this protein; it can be done in several ways.

Ebstein's diet is as follows:

6-7 A.M.—Tea without sugar or milk, 250 c.c. Dry toast, 50 grams.  
Butter, 20-30 grams.

2 P.M.—Thin soup. Fat meat with fat gravy, 130-180 grams.  
Green vegetables. Salad. Fresh fruit (apple or berries). Light Rhine wine, 2-3 glasses. Soon after this meal, plain, strong tea, 250 c.c.

7.30 P.M.—Meat with fat (egg or fish), 75-80 grams. White bread, 30 grams. Plenty of butter. Cheese (occasionally). Fresh fruit.

The value of the Ebstein diet is usually given as protein, 102 grams; carbohydrates, 47 grams; and fat, 85 grams, or the equivalent of about 1,300-1,400 calories.

The first method of diet was that advised by Banting. It was composed as follows:

**Breakfast:** 9 A.M.—Meat (mutton, beef, kidneys, broiled fish, bacon, or cold meats), 4 to 5 ounces. Tea, without sugar or cream, 1 cup, 9 ounces. Toast (or 1 small biscuit), 1 ounce.

**Dinner:** 2 P.M.—Lean meat or fish, 5-6 ounces. Vegetables (any kind except potatoes, carrots and parsnips). Dry toast, 1 ounce. Fruit (cooked, but unsugared). Claret, sherry or Madeira, 2-3 glasses.

*Tea:* 6 P.M.—Fruit, 2-3 ounces. Rusk (or toast) 1 or 2. Tea, without sugar or cream, 1 cup.

*Supper:* 9 P.M.—Lean meat or fish, 3-4 ounces. Claret or sherry, 1-3 glasses.

Banting lost 35 pounds in ten months on this diet, and his health was improved. This diet represents about 172 grams of protein; that is to say, almost 30 grams of nitrogen had to be excreted by the kidneys per day. Fats, and the readily oxidizable carbohydrates were much diminished, and alcohol—3 glasses of wine—was given. This is an additional objection. The alcohol is readily oxidizable, and consequently the fat is not so easily destroyed.

Von Noorden also had a method in which the caloric intake was cut down to about one-fifth, and the treatment continued for a long time, the monthly loss in weight being not more than three or four pounds. This is sufficient for those who have to work very hard while undergoing the cure.

He has a second method wherein the diet is cut to 1,400 calories, whereby he expects the patient to lose from four to six, and later two to four pounds per month.

Probably the better method is Umber's, who advises the "Skeleton Diet" (about 880 calories), containing 93.7 grams of protein, with the addition of various accessories, most of which are carbohydrate, to make up the calculated amount:

*Morning.*—Coffee or tea, 200 c.c., with milk, 20 c.c.; Simon's bread, 50 grams, or white bread, 30 grams.

*Forenoon.*—Fruit, 100 grams.

*Noon.*—Roast meat, 200 grams; green vegetables boiled in salt water, 200 grams; fruit, 80 grams.

*Afternoon.*—Coffee, 150 c.c., with milk, 20 c.c.

*Evening.*—Meat, 100 grams; green vegetables, 100 grams; Simon's bread, 20 grams; tea, 200 c.c.

*Bedtime.*—Fruit, 100 grams.

#### *Accessory Diet* (Each Portion = 100 Calories)

Roast beef, 80 grams; oysters, 200 grams; white bread, 40 grams; graham bread, rye bread or Zwieback, 20 grams; butter, 12½ grams; Swiss cheese, 20 grams; sugar, 25 grams; potatoes, 100 grams; rice, peas, beans or buckwheat, 30 grams; flour, 20 grams; apples, 200 grams; apple sauce, 150 grams; cranberries, 500 grams; milk, 150 grams; wine, 150 grams; brandy or whiskey, 30 grams.



*Accessory Diet of Filling Foods of Low Caloric Value*

100 grams cooked	asparagus	=	43	calories
" "	green beans	=	20	"
" "	green peas	=	108	"
" "	tomatoes	=	20	"
" "	spinach	=	52	"
" "	turnips	=	40	"

In Locke's<sup>8</sup> experience, the following menu fulfills all the above requirements very satisfactorily:

*Breakfast.*—Cup black coffee (with milk, but no cream or sugar).  
Raw fruit (1 orange, apple, pear, or  $\frac{1}{2}$  grapefruit).  
Eggs (one or two, boiled or poached). Toast (one or two small slices, i. e., 10-20 grams, usually without butter).

*11.30 A.M.*—Cup bouillon, 250 c.c. skimmed milk or buttermilk, or fruit.

*Luncheon.*—Clear soup, 120 c.c. Moderately lean meat or fish, 100 grams, (or eggs). Two varieties green vegetables, 50-100 grams each. Raw fruits.

*5 P.M.*—Tea without cream or sugar. Small slice toast, 10 grams.

*Dinner.*—Raw oysters. Moderately lean meat or fish, 100-150 grams. Two varieties green vegetables, 50-100 grams each. Salad (fruit or vegetable) with small quantity of French dressing. Raw or unsweetened cooked fruit. Demi-tasse black coffee.

The above menu represents, according to the choice, a maximum and minimum value as follows:

	<i>Protein</i>	<i>Fat</i>	<i>Carbohydrates</i>	<i>Calories</i>
Minimum	60	50	70	1,000
Maximum	100	70	165	1,738

## FOODS ALLOWED

*Meats and Fish:* All lean meats and fish, except as noted below but without rich dressing or sauce.

*Thin Soups:* In moderation.

*Eggs:* In any form, except scrambled, fried, and omelette.

*Fruits:* All fresh varieties (except bananas), and berries (without cream and sugar); cooked, if with saccharin.

*Vegetables:* String beans, water cress, lettuce, radish, cucumber, asparagus, green peas, Brussels sprouts, cabbage, cauli-

flower, okra, onions, celery, tomato, artichoke, spinach, 1 white potato, mushrooms, squash, beets, turnips, carrots, parsnips, oyster plant, vegetable marrow (cooked with but little butter and no cream).

*Miscellaneous:* Tea, coffee, skimmed milk, lemonade (with saccharin), ginger ale. Desserts made of gelatin, or Irish moss, if with but little sugar; use saccharin or saxin in place of sugar.

#### FOODS TO BE AVOIDED OR GREATLY RESTRICTED

*Starches:* Cereals, macaroni, vermicelli, spaghetti, sago, tapioca, cornstarch, sweet potatoes, shelled beans, dried peas or beans, corn, and nuts.

*Sweets:* Sugar, candy, dried fruits, syrups, fruit preserves, honey, marmalade, and sugar sauces.

*Meats:* Pork, bacon, goose, sausage, croquettes.

*Fish:* Shad, fresh salmon, eels, sardines, mackerel, bluefish. Fried fish.

*Fats:* Cream, olive oil, bacon, lard; fat meats and fishes.

*Desserts:* Ices, rich puddings, cake, and gingerbread.

*Miscellaneous:* Chocolate, alcoholic beverages, thick soups, milk, cheese, pickles, and condiments.

Any of those diets will achieve the desired result if care is taken to oversee the patient. It cannot be emphasized too strongly that the **reduction should be constantly controlled**, and equally important with the reduction of food is the **increase of exercise**.

The **blood-pressure** is usually up, from 145 to 160, and care should be taken to **observe it** and also to **examine the cardiocirculatory renal systems** from time to time.

Folin and Denis<sup>4</sup> have made an interesting contribution to the dietary reduction of obesity that is quite comparable to the methods employed in the treatment of diabetes. The danger signals of imperfect oxidation of the bodily fat will probably be the findings of *acetone bodies in the urine*. When this occurs, **the severity of the diet should be moderated** until these bodies disappear from the urine. If the strict diet is then resumed, acetone will appear much later than it did in the first instance, and a similar resumption of the higher caloric diet will lead to its early disappearance.

**TREATMENT OF SYMPTOMS.**—The principal symptom that will occasion treatment is *dyspnea*. In the early stages of the dietary treatment, dyspnea may be helped by **tincture of digitalis** in doses of 2 c.c. (½ dram) twice a day, for three or four days at most.

**HYDROTHERAPY: MECHANOTHERAPY.**—Almost every kind of hydro-

therapy and mechanotherapy has been advocated for the treatment of obesity. Most of these are successful to a certain degree, but the experience of the orthopedic surgeons gained in the treatment of nerve injuries (and this has been well upheld in the treatment of the wounded in the War), that **voluntary muscle exertion** is much more efficacious than that stimulated electrically or by massage, is of service to us here. Teaching the patient exercises that he can perform by himself accomplishes two ends. First of all, it demands a great amount of will power. Secondly, the resulting oxidation of tissues and muscular development is much greater than can be obtained when the patient is treated passively. At the same time, there are many who at first are unable to take the active muscular exercises. A great deal can be done to assist their wellbeing by **brine baths**, or **electric light baths**, combined with **massage and the Bergonie treatment**. The latter seems to have been eminently successful. The patient has numerous electrical impulses sent to all parts of the body by a mild faradic current, so that the muscles are stimulated to contract at about the same rate at which the heart beats. This results in movements that are uniformly distributed and greatly improves the circulation. The treatment should be, at first, about 20 minutes in duration, then increased to 45 minutes, and carried out about every other day.

**ORGANOTHERAPY.**—A careful use of **thyroid extract** is of great assistance in the treatment of obesity. However, too much caution cannot be exercised in its administration. Very serious results have followed the use of it by patients who have taken it, not realizing the possible dangers that may happen to the general circulation.

It is well to start with a small dose. The patient should be instructed to count his pulse for one full minute, morning and evening. He should be warned to advise the physician at once, should the pulse rate rise more than ten beats per minute. The patient should start with a dose of 0.1 gram ( $1\frac{1}{2}$  grains) three times a day. If his weight is over 200 pounds, the dose might be as much as 0.2 gram (3 grains) of the dry gland substance. As so many manufacturers put up thyroid preparations, care should be taken that the tablet does contain a definite amount of dry thyroid gland substance, and not that of the fresh gland. Should there be no effect from this dose, it may be increased, with careful observation, up to 0.3 gram (5 grains). Not only should a **chart** be kept of the **patient's pulse rate**, but his **heart should be examined** from time to time, and the **eyes investigated** for the various manifestations of hyperthyroidism, and **the hands for tremor**.

**EXERCISE.**—In all the resorts, emphasis is placed upon **walking** as an essential part of the treatment. In a great many instances, this type of exercise alone is sufficient. It can be varied, and should not be carried out on city streets. It is best done by having the individual start on the level, and if the available country is hilly enough, gradually change from the level to increasing grades. Care should be taken not to make the walking mechanical; that is to say, the same ground should not be covered twice the same day if such a procedure can be avoided.

Gradually, the country chosen should be so rough that one is unable to think of anything but choosing one's path while out for exercise.

**MEDICINAL TREATMENT.**—The medicinal treatment of obesity is unsatisfactory. Really **no drugs** have been found to be of any particular benefit.

**Prognosis.**—The patient suffering from obesity due to dietetic errors and indiscretion will recover if his mode of life and habits of exercise can be improved. He must resign himself to forego the highly concentrated foods which he has been taking, and to give the muscles much more work.

In the glandular cases, the giving of extracts of the various glands frequently ameliorates the condition.

Death is apt to occur from apoplexy, angina pectoris, syncope and acute infections, particularly of the respiratory tract, and in an essential major operation, such as appendectomy or hernia. The newer methods of anesthesia, particularly with nitrous oxide and oxygen, have resulted in some improvement in the mortality from operative procedure and the risk of lung infections dependent upon these interferences.

The accompanying table, compiled by Axtell,<sup>5</sup> from the Prudential Insurance Company's statistics, shows the effect of overweight upon the expectation of life. There can be little better evidence than these statistics, compiled from many individuals, that overweight is a serious matter.

TABLE 1.—EFFECT OF OVERWEIGHT UPON THE EXPECTATION OF LIFE, SHOWING RELATION OF DEATH RATE TO AGE AND WEIGHT

Weight above Ideal for Age:	5-10 Lbs.		15-20 Lbs.		25-45 Lbs.	50-80 Lbs.
Age	Death rate		Death rate		Death rate	
	Below Standard	Above Standard	Below Standard	Above Standard	Above Standard	Above Standard
20-24	4%	....	4%	....	1%	3%
25-29	7%	....	10%	....	12%	17%
30-34	1%	....	14%	....	19%	34%
35-39	0%	....	....	1%	31%	55%
40-44	0%	....	....	10%	40%	75%
45-49	....	3½%	....	9%	31%	51%
50-54	....	2%	....	21%	24%	49%
57-62	....	2%	....	25%	12%	38%

**Pathology.**—The most noteworthy change is the great increase in fat throughout the body. Normally, fat may be from ten to twenty per cent. of the total body weight. In the obese, it is conceivable that the weight of fat goes up to even more than half of the total weight.

It must be remembered that not only is the deposit excessive in  
VOL. IX.—4.

visible areas, but the internal organs normally containing quantities of fat in health are greatly embarrassed by the enormous increases, and organs nominally containing no fat may be quite incapacitated by the infiltrations. The face is rounded; the chest becomes very bulky; waist, abdomen and hips are large. The abdomen may be even pendulous, and the limbs greatly increased.

The heart muscle early shows infiltration and, later, replacement of the muscle fibers to fat globules. Histologically, the differences in size and number of the fat globules are marked. There is evidence of mitosis in the cells in all new areas. The fat of the blood is increased. The fat deposited even in the liver exhibits unspecialized characters; that is to say, it has not undergone its peculiar chemical processes, whereby the hydrogen atoms are removed, so that the material is more readily available for vital processes.

Leathes<sup>6</sup> has shown that fat deposited in the various storehouses is much less easily workable than the material found in the liver. When the liver is infiltrated in the obese, the character of the fat forming the increase is that of a warehouse, scattered normally throughout the body.

The acid figures and iodine principle, which are normally high because of this removal of hydrogen atoms from the molecule in the fat of normal liver, are, in the fat of the livers of the obese, much reduced. This is tantamount to saying that the liver has not only become a manufacturing area for fat, but also a storehouse.

FAT METABOLISM.—The fat of the body is derived from the food intake. Should this food intake be high in fat, it is digested by the various enzymes of the body by lipase, with the aid of pancreatic juice and bile. It is then absorbed by the epithelium of the intestine—the fatty acid, either as a water soluble soap combined with alkali, or with bile salts to form a combination that is also soluble. The glycerin, which has been split from the neutral fats of the food, is likewise absorbed, and in the epithelium is combined again with the fatty acids, and then the new compound of body fat is carried by the lymphatics to the thoracic duct.

It had been argued by histologists that the fats were absorbed as very finely emulsified droplets, and the question naturally arises as to why they are split so far and then built up again so soon after their absorption. The process is analogous to that found in digestion of proteins. It permits of a rearrangement of fatty acid molecules, so that the newly formed fat is more like the characteristic fat of the animal that is going to use it. Bloor<sup>7</sup> has shown that the chemical properties of the fats are very much changed in digestion. For example: when fat with a high melting point is fed, that recovered in the thoracic lymph is changed to one of distinctly lower melting point, and *vice versa*. The intestine then possesses the power to modify the composition of fat during its absorption. The time taken is remarkably short. By Bloor's methods, the fat of blood of the dog (which is very

uniform) is found to increase after a fatty meal, within one hour, and to reach its maximum in about six hours.

The blood fat is transported to three places: first, the tissues; second, the liver; and third, the depots for fat. These three areas are characterized by fats different in composition. If no active metabolism is going on, that of the liver is like that found in the tissues, but when active metabolism is taking place, the liver fat occupies an intermediate position. The depot fat is found in the subcutaneous and retroperitoneal tissues, and it is these areas that exhibit such great augmentations in obesity. All fat is not derived from the fat of food, but partly from the carbohydrate. That in the depot may be easily prepared for use in the organism, or with difficulty. If the latter, it is taken up very slowly, and again prepared for use very slowly. This is a further proof of the contention that sufferers from obesity should not be allowed to lose weight rapidly.

The fat in the liver is a different material from that in the depots. It is available for energy. MacLeod<sup>8</sup> has compared it to explosives. In the depots it is the raw material; in the liver it is like wet gunpowder. It contains much potential energy, but when it is dry in the liver, it is sent to the tissues to be exploded.

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## CHAPTER III

### LIPOMATOSIS

BY WILLIAM FLETCHER MCPHEDRAN, B.A., M.B.

Etiology, p. 53—Symptomatology, p. 53—Clinical history, p. 53—  
Physical findings, p. 53—Diagnosis, p. 54—Clinical varieties, p.  
54—Treatment, p. 55—Pathology, p. 55—References, p. 55.

**Etiology.**—The disease usually occurs about middle life in the great majority of cases. Many of the individuals have a bad family history of insanity. Worry and injury are also considered predisposing causes.

**Symptomatology.**—**CLINICAL HISTORY.**—*Mode of Onset.*—The disease begins in a slow, insidious manner. Large numbers of isolated, fatty tumors are found distributed in different parts of the body. They usually start singly over the trunk or on the extremities. They may be the first sign of an over-production of fat, or may be found in a person who has for some years weighed too much. Areas of tender swelling, irregular in size and shape and in their location, are found. They may measure from five to ten centimeters in diameter; they are raised above the surrounding tissue, whether it is fatty or approximately normal. The skin over them may show slight evidences of inflammation; it may be reddened, congested, and perhaps a little edematous, but very rarely are the vessels distended. The areas are usually exquisitely tender, and the patient has burning or sticking sensations of pain, even when these areas are not manipulated.

*Symptoms during Progress of Disease.*—In a few days the inflammatory reaction subsides, but the hardened area in the fat tissue remains. It is still painful and tender on manipulation. The process is repeated from time to time; sometimes in a new area, but it may be that an old one is affected anew. The face, hands and feet are never affected.

In the later stages of the disease, the fat may not be a predominant symptom of the tumors. It is usually confined to large masses surrounding the fatty tumors of the trunk and extremities. Occasionally there may be no tumors at all, but merely the development of areas of fat that are tender on palpation.

**PHYSICAL FINDINGS.**—Pain is the most predominant symptom, and may be experienced before the development of tumors. While it has been supposed, from their universal distribution and from the fact that often the patient has locomotor ataxia or other cerebrospinal disease associated with the fatty tumors, that the disease is primarily of the nervous system, the pain of which the patient complains does not usually follow nerve trunks, nor is there any tenderness on palpation.



over the nerve trunks. Pain and tenderness may be brought out, or increased, by means other than pressure. Heat or cold may be experienced as pain by the sufferer, where in the normal individual no such effect would be noticed. Another common symptom is weakness. There is loss of appetite; the patient loses energy, is apathetic and sluggish, and mental symptoms corresponding to these are most common. The apathy and psychic depression, with hallucinations and dementia, may be so severe as to render commitment to an institution necessary.

In Dercum's original case, there were areas of anesthesia interposed between the areas of tenderness and hyperesthesia. In this case, too, there were evidences of marked disturbance of the autonomic nervous system. Scleroderma of the extremities, dermographia, ulcerations of the skin, and disturbances in sweat secretion were found.

**Diagnosis.**—The diagnosis is usually fairly simple. Care must be taken in the earlier stages of the disease to differentiate it from *chilblains* and *mild frostbite*. In these patients, the absence of exposure, age, and usually the tendency to obesity, will help in their differentiation.

**Clinical Varieties.**—Various localized collections of fat, or even of edema, may be mistaken for the typical lipomatosis or *adiposis dolorosa*.

1. **DIFFUSE SYMMETRICAL ADENOLIPOMATOSIS.**—Diffuse symmetrical adenolipomatosis of the neck was first described by MacCormac<sup>1</sup> and consists of large symmetrically placed fat masses in the neck, axillæ and trunk. There is no tenderness. The patient suffers from asthenia, mental irritability, apathy and depression, and enlargement of the spleen. His pulse is fast. Even when the fat masses are large there may be emaciation. The name adenolipomatosis was given because the individual was found to have small areas of sclerosed glandular tissue scattered throughout the fatty masses. At first, and even occasionally throughout the disease, the individual may have good health. Then the tumors are disfiguring rather than pathogenic.

2. **ADIPOSIS TUBEROSA SIMPLEX.**—This term was used by Anders<sup>2</sup> to describe patients who had masses of fat resembling Dercum's disease, yet the masses differed in their formation, distribution, and in the manner in which they yielded to treatment. The masses in this variety of lipomatosis are generally found in the abdominal wall, and the patients are obese.

3. **MULTIPLE LIPOMATOSIS.**—Large numbers of tumors may be found scattered all through the different parts of the body. Because they were symmetrically arranged, and followed the nerve trunks, it was thought that they were of a nervous origin, particularly as they were often found with *tabes dorsalis* or general paresis. No substantial evidence has ever been brought forward to support this view.

4. **CEREBRAL ADIPOSITY.**—The condition of *dystrophia adipose-genitalis* of Fröhlich, while attended in the major portion of the instances with general adiposity, may be associated with tumor formation. It is now generally known that these cases are due to a fault in the region of the *hypophysis cerebri*.

5. **PSEUDOLIPOMA.**—Sydenham described the swellings in hysterical

patients that left no impress with the finger, nor any mark. These are found in the neck, and disappear.

**Treatment.**—Unfortunately, very little indeed can be done in the way of making the patient's life happier. In the treatment for the prevention of overweight, and hardening of the fatty tissues, particularly the thyroid gland therapy has met with some success. **Acetosalicic acid and salicylates in general** have been used for pain with indifferent success. Occasionally some of the tumors have been **excised**, but while this method of treatment has removed the offending area, new ones have been found to develop easily.

**Pathology.**—Numerous fatty tumors are found scattered all over the body, except on the hands, feet and face. The number in one individual may be very high, perhaps as high as two thousand. The tumors are simply pads of fat. No reason, from a pathological or etiological standpoint, has yet been advanced for the marked tenderness and pain.

Usually lesions have been found in the various glands of internal secretion. Tumors of the pituitary gland are the most frequent, but occasionally, as in McCarthy's case, there may be a tumor of the thyroid gland. Other cases have been reported where the tumors have been in the dura mater, and others occurred in the wall of the ventricle. They have blocked the bundle of His, and led to a development of heart block.

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## CHAPTER IV

### HEMOCHROMATOSIS

By WILLIAM FLETCHER MCPHEDRAN, B.A., M.B.

Etiology, p. 57—Predisposing causes, p. 57—Symptomatology, p. 59—Physical findings, p. 59—Laboratory findings, p. 59—Diagnosis, p. 60—Treatment, p. 60—Prognosis, p. 61—Pathology, p. 61—References, p. 63.

**Etiology.**—PREDISPOSING CAUSES.—Various hypotheses as to the causation of hemochromatosis have been advanced from time to time. It has been supposed to be due to a primary destruction of blood, resulting in the deposition of pigment and sclerosis; to universal abnormalities of the metabolism of individual cells or to specialized abnormalities of their chromogenic activities; to abnormal autolysis of the liver cells similar to that believed to occur in diabetes by some writers; to primary cirrhosis of the liver, and then a secondary hardening of the pancreas. Von Recklinghausen described the disease first, laying particular stress upon the primary blood destruction. This he thought resulted in the deposits of pigment all through the body. Occasionally other evidences of blood disease have been noted in the cases studied. Opie observed purpura in four cases; Potter and Milne, tuberculosis; Sprunt, a history of dysentery; and Osler and Rolleston, a history of malaria. But while anemia has been described, it is rarely found.

The most interesting fact in connection with the relationship to blood diseases is that excess of urobilin output in the urine and feces has not been described, and no observation has been made of changes in the blood-forming organs that would indicate a rapid manufacture to replace a loss. Abbot has observed that this simple blood destruction alone could not account for the deposition of pigment, but thought that the pigment which was set free caused inflammatory reactions in all organs of the body.

Recently Gaskell *et al.*<sup>1</sup> reported a case in which they studied the metabolism and found that there is an increased amount of iron in the blood. They also found the increase of hemosiderin of the distinct convoluted globules in hemochromatosis, and in the proximal in pernicious anemia. From this, they argued that hemochromatosis was the result of a defective elimination.

Sprunt, Colwell and Hagan<sup>2</sup> supported the theory of autolysis. They placed the liver of a rabbit in an aseptic chamber, and incubated it, and found that iron-containing and other pigments were to be found in the cells on autolysis, even after all hemoglobin had been removed

from the specimen. Howard and Stevens<sup>3</sup> found a slight, but definite, retention of the iron in the blood. In their case there was no increase in the amount of urobilin found in the urine in life. The amount of iron in the liver, they calculated, was at least one hundred times the amount found in the whole body under normal conditions. In spite of this great increase, however, there was no rise in the amount in the blood. At the rate of retention that they observed, it would take the liver forty years to retain the amount that was found in it by them. While this is a possible explanation, it is hardly likely, when one remembers the amount in the blood was on the lower level of normal values.

Similar observations have been made by Muir and Dunn.<sup>4</sup> They pointed out that the food is the sole source of iron, and that the daily intake is not more than 30 milligrams. If this amount were totally retained, it would take three years to accumulate the quantity found in the liver in hemochromatosis.

The French observers, notably Hanot and Chauffard, thought that the pigmentation of the liver was due to nutritional changes from the inflammation of the endarteritis associated with diabetes. They thought that the blood destruction was the first stage of the disease, and that the chronic pancreatitis caused characteristic symptoms of diabetes to develop. Potter and Milne were of the opinion that every case of liver cirrhosis might lead to hemochromatosis, because hemosiderin was to be found deposited in the tissues somewhere in the body, and that hemochromatosis was merely an exaggerated stage of this universal process. McCreary<sup>5</sup> considered blood destruction to some degree a factor in the production of the disease, because the blood examinations were done only in the latter stages, and so would not represent the true state of affairs for long periods. He notes the selectivity of the iron deposition: little is found in the kidney, a great deal in the liver.

Some experiments of Rous and Oliver<sup>6</sup> shed a great deal of light on the subject. They transfused rabbits six days in the week, for months at a time, and found the same conditions as existed in hemochromatosis, and in this disease alone, except that neither diabetes nor hardening of the pancreas was found in any rabbit. The changes in the rabbit were much less marked than those in the human being, because the process never went so far as to endanger the animal's health. Even the skin was found to be brownish in tint, and to contain hemosiderin in the deeper layers. The relationship of the disease to cirrhosis of the liver is interesting when viewed side by side with the specimens from the rabbit. They were killed at a relatively early stage of pigmentation, and Rous points out that at the outside of the liver lobules, the parenchymal cells were much pigmented, but had not broken down; hence, although these heavily pigmented cells had induced atrophy in those surrounding them, there had been no connective-tissue reaction replacing them. While it is possible that the connective-tissue proliferation might have followed any time, it hardly seems likely when one remembers that an immediate reaction was not observed; that is to say, that the hemo-

siderin did not produce any stimulative effect on the interlobar tissue.

Rous was fortunate enough to have a patient in the earlier stage of the disease, and found that the cells at the periphery of the liver lobule alone were pigmented as much as the rabbit's. But even at that stage of pigmentation, cirrhosis was very marked, so he was led to the conclusion that the cirrhosis was the primary cause of the disease. He found, however, from the rabbit material, that where the tendency to pigmentary deposition exists, an intercurrent proliferation of connective tissue will increase the deposition of pigment. One of the animals subjected to repeated transfusions had had a lesion of the peritoneum on the liver. In that area, there was a great increase in the amount of pigment deposited.

The diabetes with all its sequelæ is explainable on the basis of the destruction of pancreatic tissue.

**Symptomatology.**—Most of the cases of this disease that have been reported have been in men of from forty to fifty years of age. Frequently they have been hard drinkers of spirits and have experienced the various manifestations of indigestion. It is probable that these two items in the history are not without interest, when one considers the amount of cirrhosis of the liver that is found at autopsy. The change in color starts to be noticeable in the areas that are normally pigmented, that is to say, those uncovered by clothing and the folds of the axillæ. As a general rule, however, the sufferer from hemochromatosis makes no complaint as to his health while this gradual change in color is progressing. In the more marked cases he may observe that he is not quite so strong as he was and that he is losing a little weight. Frequently an examination of the urine made at this time has shown that there are evidences of nephritis long before the onset of the diabetes associated with the change in color. But with the development of the diabetes, the subjective phenomena are those of diabetes alone. Patients experience thirst, voracious appetites, polyuria, and pruritus. Several cases have been reported in which no diabetes was found at any time. In them the patients have been almost free from subjective symptoms.

**PHYSICAL FINDINGS.**—The appearance is very striking—the likeness to an Egyptian mummy has struck many. The skin of the face and hands is bronzed; all over the body it is much darkened, of an iron-gray color, but this darkness is not uniformly distributed. It is patchy or mottled, thin bands joining up larger areas that are oval or roughly circular, the latter having no outline. The change in color is more marked where color is found in health. It is believed that the mottled appearance is due to the deposition of the pigment in the areas of vascular congestion or reduced circulation. Usually none is to be found in the mouth cavity. Often there is tenderness over the abdomen, particularly over the liver and spleen. The liver is usually small. There is most often some free fluid in the abdominal cavity and edema of the extremities is present. The amount of subcutaneous fat is greatly reduced all over the body.

**LABORATORY FINDINGS.**—*Blood.*—The blood is normal. The number

of red blood-cells is seldom reduced. The hemoglobin ranges from 72 to 95 per cent.

*Urine.*—The urine is increased in amount; it most often has the characters of severe diabetes, high in specific gravity, containing a varying amount of sugar, and often diacetic acid.

Rous<sup>7</sup> has advised the method of examination of the urine that promises to render the removal of portions of the skin for the diagnosis of hemochromatosis unnecessary. This consists in the examination of the urine for hemosiderin crystals. A perfectly fresh specimen is centrifuged; the sediment is then gone over for any suggestive orange or brown granules, which will probably be found in the epithelial cells or in casts. The fresh sediment is mixed with a little human serum (absolutely free from hemoglobin) and thick films are made. These are fixed by heat, placed in strong ammonium sulphide for one hour, washed with water and treated with a fresh mixture of 2 per cent. potassium ferricyanid and 1 per cent. hydrochloric acid in equal parts. The film is then rinsed again, and stained with lithium carmin for a few minutes, then differentiated in 1 per cent. hydrochloric acid alcohol, and run through 95 per cent. alcohol, absolute alcohol xylol, and mounted in balsam. The acid alcohol turns the iron granules a deep blue, and if carried on too long, may dissolve out this blue color. It also helps to differentiate the carmin in the cells. Permanent mounts can thus be obtained and studied at leisure. Rous has used this method in several cases of pernicious anemia, and found granules in several of the cases, but in the one case of hemochromatosis studied the granules were present in large numbers, often as large as big corpuscles. Over forty patients were examined in this way for iron, and none was found. The reaction was only brought out in specimens obtained from patients ill with pernicious anemia or chronic hemolytic jaundice, in addition to the case of hemochromatosis that he studied.

*Skin.*—The diagnosis is most often confirmed by snipping out, under local anesthesia, a small piece of the skin. The piece is hardened in alcohol, and sectioned. It is then stained with 2 per cent. ferrocyanid of potassium for one hour, transferred to 1 per cent. hydrochloric acid for one hour, and counterstained with alum-carmin. The characteristic Prussian blue color of the tissues is then easily observed.

*Diagnosis.*—Hemochromatosis must be diagnosed from *Addison's disease*. Here the spleen and liver are not enlarged. There is pigmentation of the mouth, and no glycosuria. The finding in the urine of hemosiderin crystals, as outlined by Rous, is of great importance. From *jaundice*, it can be differentiated by the absence of yellowish color of the conjunctiva, and from *argyria* by the history.

*Treatment.*—Treatment has been unsatisfactory in all cases. The cirrhotic condition of the pancreas is further accentuated by a deposit of pigment, and while an effort should be made to treat the individual on the lines laid down by Allen, in numerous articles on diabetic treatment, it is improbable that the patient will do well.

**Prognosis.**—The prognosis is bad. All cases have succumbed after about two or three years of life.

**Pathology.**—**MACROSCOPIC FINDINGS.**—There is marked thinness and emaciation of all the tissues. The heart is usually flabby and tends to alter its shape when placed on a flat surface. There are fatty spots to be found on the papillary muscles, giving it the appearance of a thrush's breast.

**MICROSCOPIC FINDINGS.**—On microscopical examination, the heart muscle is found to be very pale, and the fibers are narrow, many of them being broken up, either irregularly or in segments. There is no evidence of an inflammatory change, but the muscles are loaded with a brownish pigment within their substance. This pigment is arranged around the nucleus, and in the form of a wedge, of which the nuclear membrane is the base. This golden-brown pigment is believed to be hemofuscin. Another kind of pigment is found in the myocardial tissue. It is usually in between the fibers, and particularly around the smaller blood-vessels. It is coarser, and more intense in its natural color, than described above. When one tests for iron (by the Nishimura method), one finds that the latter pigment gives the iron reaction upon which the essential points in the diagnosis of hemochromatosis depend. The pigment in the heart muscle fiber itself is probably that of brown atrophy, whereas the rest is iron-containing, and found in a few diseases. In many instances the amount of pigment is so great that when stained by the Nishimura method, the section appears bright blue in the gross.

**Circulatory System.**—The arteries are not much changed. Occasionally one would expect to find the endarteritis obliterans of diabetes in cases that have had diabetes for a considerable time before death.

The lymphatic glands are usually infiltrated with the red-yellow pigment deposited in rough granules, irregular in size and shape. The pigment usually lies between the connective-tissue cells. In many cases, the growth of pigment and connective tissue may be so great that the gland loses its normal structure. The pigment is deposited often in layers, that towards the center of the granule being much firmer in consistency and staining qualities than that on the outside of the granule.

**Respiratory System.**—The lungs are usually free from pigment.

**Digestive System.**—The stomach and intestines usually contain iron-staining pigments in the walls. None is found in the epithelial cells or in the deeper structures, but it is confined to the interstitial tissue under the epithelium.

*The liver* usually weighs about 1,500 grams. There may be some old inflammation of the peritoneum. It is smooth, and often greatly increased in connective-tissue formation. All stages of cirrhosis, from very slight infiltration of the connective tissue to the most advanced degrees, may be found. On sectioning, the picture is that of cirrhosis of the liver, with great increase of the septa, and the blood-vessels are found prominent here. Quite often newly-formed bile capillaries may be seen coursing through the areas. The pigment is easily noticeable, present in large quantities, either as finely scattered grains all over



the surface or perhaps run into bigger masses in various areas. The areas may be so large that the liver cells are completely crowded out, but as a general rule, the pigment is arranged around the periphery of the lobule, surrounded by the cirrhotic process. Almost all the cells contain some pigment. It tends to be found in the part of the lobule farthest away from the blood capillary; all cells take the iron stain deeply. The iron-containing pigment is also found in the fibrous tissue, and in the walls of the larger blood-vessels.

The general view of the liver is then, that the iron pigment is accumulated in the liver cells around the bile capillaries. From this accumulation, atrophy of the liver cells and chronic inflammatory proliferation of the fibrous tissue septa occur. Not only is the iron-staining material found stored, but it is seen in the cells circulated in the capillary blood-vessels. Areas of regeneration are commonly observed.

*The pancreas* is usually the seat of a chronic inflammation. It is adherent to the surrounding structures, softened often, or it may be hardened from the excess growth of connective tissue. This connective tissue may serve to differentiate the lobules from one another, or may be very marked and diffuse all through the lobular areas. Areas of necrosis are usually easily found. The islands of Langerhans are most often completely destroyed. Not only are the islands the site of a marked pigment infiltration, but very often they are found to contain masses of fat and great amounts of the pigment; but on the other hand, almost every cell in the pancreas will be found to contain iron-staining material to some degree. The areas of fibrosis are conspicuous for the large amount that they hold.

*Genito-urinary System.*—The kidneys usually weigh about 600 grams, and frequently they are the site of abscesses due to a terminal septicemia. On sectioning, the glomeruli are large, congested, and often show evidences of fatty change. The tubules are large, and stand out conspicuously in the section stained for iron, as the protoplasm contains a great deal of this pigment. Usually this pigment starts just as the tubule emerges from the lobe of Henle. The pigmentary deposit is confined to the second portion of the convoluted tubule—that is, after it has passed out of the lobe of Henle. It is also found to some extent in the glomerulus. Gaskell regarded this as further proof of the hypothesis that the glomerulus excreted the urine and the convoluted tubule of the second order absorbed certain constituents and rendered the product more concentrated.

*Diseases of the Ductless Glands.—Spleen.*—Various tissues are fairly well preserved, except that there is a diffuse increase in the fibrous tissue. There is a diffuse pigmentation all over the organ.

Areas snipped from the skin show the epidermis much thinned. There is usually no fat from the subcutaneous tissues because of the diabetes. In the epidermis, there is a great collection of pigment in brown granules, also in the corium, but the most abundant deposit is in the deeper layers of the skin, around the sweat glands. Here it is gathered into large masses that tend to run in bands. If these sections

are stained by the iron selective stain it is found that only the material in the deeper layers takes the iron stain.

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## CHAPTER V

### OCHRONOSIS

BY WILLIAM FLETCHER MCPHEDRAN, B.A., M.B.

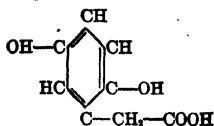
Etiology, p. 65—Symptomatology, p. 65—Laboratory findings, p. 65—Diagnosis, p. 66—Treatment, p. 66—Pathology, p. 66—References, p. 67.

**Etiology.**—The cause of ochronosis is the deposition of pigment in the cartilages. It is probable that this ochronitic pigment is circulating in the blood stream as a mother substance and is precipitated in the cartilage. There are several instances where the long-continued use of dilute carbolic acid solutions has led to a similar deposition of pigment.

**Symptomatology.**—The patient may be led to consult a physician, because, on medical examination for life insurance, a reducing substance was found in the urine. This substance is the rare homogentisic acid, the cause, not only of alkaptonuria, but probably also of ochronosis.

The subject may occasionally have experienced discoloration of the clothing from this sporadic pigment in the urine. In marked cases the concha of both ears is bluish-gray, and this pigmentation is increased on illumination; it is universally distributed through the ears, and has no relation to the skin. The eyes show deep black color in the exposed white portions. Interspersed in these areas of black are areas that are normal in color. This color tends to become darker as time goes on. The tarsal cartilages are not affected. Over the nose and cheeks the skin is coal-black in color. Osler<sup>1</sup> thought, at first, that it looked like a large number of irregularly placed comedones. The line over the nose is narrow, but widens as it passes to the cheek, and over the malar prominence there is a butterfly distribution. There is no thickening of the skin.

**LABORATORY FINDINGS.**—In the majority of cases reported, the urine has exhibited the phenomenon of alkaptonuria. This is the most important of the amino-acid disturbances in metabolism that have been investigated. When passed, the urine is of normal color, but turns dark brown, either on the addition of alkali or on the absorption of oxygen on standing. The body responsible for this is homogentisic acid:



Homogentisic Acid

As much as seven to twenty-five grams of this acid may be excreted daily. Of the 25 cases reported by Poulsen,<sup>2</sup> 12 had alkaptonuria, 6 were normal, 3 were not investigated and 2 had carboluria; 5 unknown. It is probable that, as the urine in other cases contains only minimum amounts of pigment, the pigment really has been the melanin that is to be found in large amounts in outspoken examples of the disease.

Janney<sup>3</sup> has described a case of ochronosis in which extensive investigations of the metabolism have been reported. The disease had lasted eighteen months in a man aged forty years. He exhibited the bluish color of the cartilages and inflammatory reactions in several joints; at autopsy, intense black pigmentation of the bones—particularly the ribs—was found. The urine, when passed, was normal in color, but on standing became dark brown. It reduced Benedict's solution. Several attempts were made to support homogentisic acid, but none could be found. Melanin was readily procurable from the urine, and also from the cartilages and ribs.

**Diagnosis.**—The diagnosis may be established by the bluish-gray discoloration of the ear and nose cartilages and the cartilages of the eye. The importance of investigating substances in the urine which give reducing reactions with copper and by other means cannot be overestimated. No individual should be classed as diabetic until these reducing substances have been further examined.

**Treatment.**—There is no established treatment for this disease. It is possible that as the homogentisic acid comes from two other sources, tyrosin and phenylalanin, the amounts governed in the diet may be reduced in protein metabolism—they are both split off from the protein molecule—and there are certain proteins that contain them in larger amounts than others. Casein and fibrin are the most important. If 50 grams of tyrosin are swallowed by a normal individual, homogentisic acid appears in the urine. It therefore follows that if the individual can be kept on a low protein diet, it is possible the staining of his cartilages might be reduced.

**Pathology.**—The principal interest is centered around the finding of the pigment in the cartilages. The pigment is to be found in the rib cartilages in its greatest concentration; usually they are quite black. In the early stages of the disease they are probably bluish-black or blue-gray. The pigment is under the perichondrium and in the bony part of the rib, that is to say, where the blood supply is the most luxurious. The cartilages are often much hardened. Microscopically the pigment is in the ground substance, while the capsule and the cells are quite uncolored unless there has been some disease of the joint, and then the diseased portion is deeply colored.

The large joints are pigmented, while the cartilages of the smaller joints generally escape. Pigment may be found in all cartilaginous structures, intervertebral disks, and occasionally in the joint capsules. It is also found in the heart valves, and in the blood-vessels and kidneys.

The pigment is dissolved by hot potassium or soda solution, and it gives no iron reaction; the solution in alkali gives no absorption bands

in the spectrum. It is not colored by fat stains, and it is probable that it belongs to the class of the melanins. Virchow, the original investigator, thought that it was a hematin derivative, but the absence of iron reaction renders this improbable.

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## CHAPTER VI

### DIABETES MELLITUS

BY HERMAN O. MOSENTHAL, M.D.

Definition, p. 69.

Normal carbohydrate metabolism, p. 70; The blood sugar, p. 71; The normal and the diabetic blood sugar, p. 71.

Glycosuria, p. 74; Renal glycosuria, the relation of the kidney to the blood sugar, p. 74; Other glycosurias, p. 76.

Diagnosis, p. 78; The identification of glucose in the urine, p. 79; Test for carbohydrate tolerance, p. 80.

Acidosis, p. 81; Degree of acidosis, p. 86; Symptoms of acidosis, p. 91.

Etiology, p. 91.

Symptomatology, p. 94; Findings in the urine, p. 95; Results of polyuria, p. 97; Loss of weight and emaciation, p. 97.

History forms, p. 98.

Complications, p. 98.

Clinical types, p. 101.

Treatment, p. 103; Dietetic therapy, p. 104; Considerations guiding the dietetic treatment of severe diabetes, p. 109; The treatment of severe cases, p. 122.

The use of insulin in diabetes mellitus, p. 125; Effect of insulin on the carbohydrate metabolism, p. 127.

The treatment of complications, p. 131.

Course and prognosis, p. 133.

**Definition.**—Diabetes mellitus is a disease characterized by an *excess of sugar in the blood* and by a *constant output of glucose in the urine on a normal carbohydrate intake*. This definition is unsatisfactory, since it lays no stress on the cause of the condition. Whatever views are entertained in regard to the pancreatic lesions, there are no clinical symptoms that enable us to demonstrate them directly. There are instances of glycosuria in which the blood sugar is not above normal; these so-called cases of renal diabetes or glycosuria must be sharply distinguished from diabetes mellitus. Other sugars that may be confounded with glucose in the urine are pentose, lactose, levulose and maltose. These, when not accompanied by a glycosuria, constitute harmless metabolic anomalies that have no relation to the disease under consideration. Furthermore, the glycosuria must be more or less constantly present if the diagnosis of diabetes mellitus is warranted. It must be recognized that as the result of nervous shock or trauma, particularly about the head, and under other circumstances, traces of glucose may appear in the urine. If these are temporary, the patient should not be considered to be a diabetic. On the other hand, such individuals should be closely watched, as some of the severest cases sometimes first manifest themselves by showing slight glycosurias at intervals of months, and it is only after the course of several years that frank symptoms of diabetes become apparent. Finally, it must be recognized that no normal individual will excrete glucose in the urine while he is taking starch—not sugar—in any quantity whatsoever. In doubtful cases, the diet must be taken into consideration in making the diagnosis.



**Normal Carbohydrate Metabolism.**—This is so intimately associated with diabetes that a survey of this subject is not out of place. Starches ( $C_6H_{10}O_5$ )<sub>x</sub> are changed to maltose, a disaccharid ( $C_{12}H_{22}O_{11}$ ), by the diastatic ferment, ptyalin, of the saliva. The maltose is acted upon by a ferment, maltase, and becomes glucose or dextrose ( $C_6H_{12}O_6$ ). These processes are carried on in the mouth and later in the stomach, until the hydrochloric acid of the gastric juice affects the reaction of the food, when they are stopped. The amylase of the pancreatic secretion and other less important ferments complete the transformation of the starch to glucose in the intestine. The glucose is rapidly taken up by the portal circulation and transported to the liver. Here it is synthesized to glycogen, which has the same chemical formula ( $C_6H_{10}O_5$ )<sub>x</sub> as the starch of our food, but differs from it in certain physical characteristics. It is often spoken of as animal starch, in contradistinction to the ordinary starch elaborated by plants. The liver stores the glycogen. The maximal quantity which it may contain varies in different animals, being about 10 per cent. by weight in man.

From the liver the glycogen is given off to the general circulation as glucose. How this transformation is affected is not known. The liver, however, changes the stored glycogen to glucose at such a rate that the percentage of sugar in the blood remains constant at a level of from .06 to .12 per cent. By these means the tissues are furnished the necessary carbohydrate for their vital activities. Some of the glucose is not made use of immediately, but is resynthesized to glycogen, to be stored as it was in the liver. Traces of this material have been found in the leukocytes and in the placenta; the main subsidiary storehouse is in the muscles. These can take up glycogen in amount equivalent to 0.5 to 0.9 per cent. of their weight; this is an amount approximately equal to that found in the liver. The glycogen of the muscles is again changed to glucose before it is utilized. The tissues, in deriving heat and energy from the glucose ( $C_6H_{12}O_6$ ), break it down into carbon dioxid ( $CO_2$ ) and water ( $H_2O$ ). The latter may be regarded as the end products of this process; the intermediate steps are as yet not completely understood. The carbon dioxid and the water are subsequently excreted as waste products.

**Origin of Glucose from Protein—D:N Ratio.**—It is very important to realize that not only the starches and sugars may give rise to glucose, but that proteins may do this as well. Fats and alcohol will not be changed to glucose in appreciable quantities. As is well known, the proteins, on being digested, are split up into their constituent amino-acids; these in turn may be regarded as giving rise to a nitrogenous and a non-nitrogenous portion. It is the latter that is transformed into glycogen within the body. The fate of this carbohydrate is exactly similar to that which is derived from the starch of the food. The importance of proteins as a source of glucose to the body may be gathered from the fact that 58 per cent. by weight of proteins is utilized by the organism as glucose.

Lusk and his collaborators have been largely responsible for the determination of the above facts. They have carried the practical application of these findings one step further. It is readily appreciated that, if a definite amount of glucose and a definite quantity of nitrogen are to be derived from protein food, there must be a constant ratio between them. This may be expressed as the glucose or dextrose, nitrogen

ratio. The D:N ratio has been found to be 3.65:1. In every human being the greater portion of waste nitrogen is excreted in the urine; in the diabetic, the glucose which is not utilized is eliminated by the same means. Thus, if the amounts of these two substances in the urine are known, and due allowance is made for urinary sugar derived from the carbohydrate in the food, an idea may be gained from the D:N ratio in the urine as to the severity of the diabetes. The nearer the figure of 3.65:1 is approached, the more advanced is the disease. When the ratio is 3.65:1, the diabetes may be said to be complete, that is, no carbohydrate whatsoever is being utilized. Originally, this maximal ratio was designated as the "fatal ratio." This, however, is apparently incorrect, as there have been a number of cases exhibiting such a ratio which have lived for a considerable period and even become free from sugar in the urine. The best and most reliable results in the estimation of D:N ratios are obtained if the patient is on an absolutely starch-free or on a starvation diet.

**The Blood Sugar.**—This is generally considered to be glucose. It must be borne in mind, however, that the last word on this subject has not been written. Lepine has formulated the theory that the blood sugar occurs in two forms, "immediate" and "virtual." The first of these presumably is glucose, the second a more complex carbohydrate which can be measured as glucose only after boiling the blood in an acid solution. The recent work of Admont Clark, in perfusing the beating heart and pancreas with dextrose solutions, goes far to show that, at least, a part of the glucose of the blood is changed to a more complex sugar before it is finally utilized. At present, the clinician finds it impracticable to recognize any carbohydrate in the blood except glucose, and all the facts at our disposal are based on this supposition.

**TESTS FOR BLOOD SUGAR.\***—The normal amount of glucose in the blood varies from 0.06 to 0.12 per cent. The upper values are the more usual. It is within a comparatively few years only that suitable clinical methods for the determination of blood sugar have been perfected.

**THE NORMAL AND THE DIABETIC BLOOD SUGAR.**—In the *normal* individual the fats and proteins of the food will not cause a rise in the blood sugar; this is not the case in the diabetic. The ingestion of carbohydrates, especially the sugars, will result in a distinct increase in the glycemia in all individuals whether diabetic or not. This fact has assumed considerable importance, since it may be of value in making the diagnosis of diabetes mellitus in some cases. Hamman and Hirschman, in carrying out intensive studies on blood sugar, found in a normal person, after ingestion of 100 grams of glucose, a very characteristic blood-sugar curve. The 100 grams of glucose are taken as a lemonade in the morning after the night fast. The glucose is dissolved in warm water, the juice of several lemons and an orange is added, sufficient water to make the mixture up to 300 c.c. is poured in, and the whole cooled by packing in ice or adding ice before serving. With these precautions, the nausea

\* Those generally used are:

1. Benedict, S. R., Jour. Biol. Chem., 1918, xxxiv, 203.

2. Folin, O., and Wu, H., Jour. Biol. Chem., 1919, xxxviii, 81.

When only very small amounts of blood and limited laboratory facilities are available:

3. Epstein, A. A., Jour. Am. Med. Assn., 1914, lxiii, 1667.

and vomiting so frequently attending the administration of such large amounts of glucose are usually avoided.

The blood sugar of the normal individual under these circumstances rises rapidly. Usually the maximum level is attained in about 30 minutes. Rarely is the highest point in the glycemia reached later than this, though it has been observed as late as 2 hours. The blood-sugar readings never rise above 0.15 per cent. and usually return to the fasting level within one or two hours and have a tendency to become slightly lower than the control. Thus a normal blood-sugar curve following the ingestion of 100 grams of glucose has been established. The following may serve as an example:

Hour	Blood Sugar (Per Cent)	
8.47	0.101	Fasting.
9.00		100 grams glucose taken.
9.10	0.112	
9.24	0.124	
9.45	0.137	
10.03	0.096	
10.30	0.095	
11.04	0.094	
12.10	0.078	

This curve may be contrasted with that in a patient who had given evidence of *glycemia* at times:

Hour	Blood Sugar (Per Cent)	
10.50	0.078	Fasting.
10.55		10 grams glucose taken.
11.11	0.113	
11.25	0.143	
11.40	0.200	
11.57	0.234	
12.55	0.265	
2.10	0.099	

In this instance an example is furnished of what the *diabetic blood-sugar* curve is after taking 100 grams of glucose. The reaction is very much prolonged and the level of blood sugar rises to a considerably higher level. Hamman and Hirschman lay particular stress on the prolongation of the reaction. The contrast between the normal and the diabetic may be readily seen in the accompanying chart (Fig. 1).

These types of blood-sugar response to the ingestion of glucose have been given in considerable detail, as they furnish one of the most efficient means at our command of making the diagnosis of diabetes mellitus in doubtful cases. Hamman and Hirschman believe that only four venipunctures are necessary to carry out this test: the first before the glucose is given, the second one a half hour after, the third an hour after, and the fourth two hours after. Janney and Isaacson believe that the simplest form to which the technic is reducible is to determine the blood sugar during fasting and two hours after the glucose is administered, when the blood sugar in normal subjects returns to its fasting level.

The diabetic type of blood-sugar response to the ingestion of glucose is not confined to diabetes, but may be found in a variety of conditions in which there is apparently some interference with the proper utilization of carbohydrates. It is associated with overactivity of the thyroid gland and the hypophyseal gland, the injection of epinephrin, chronic

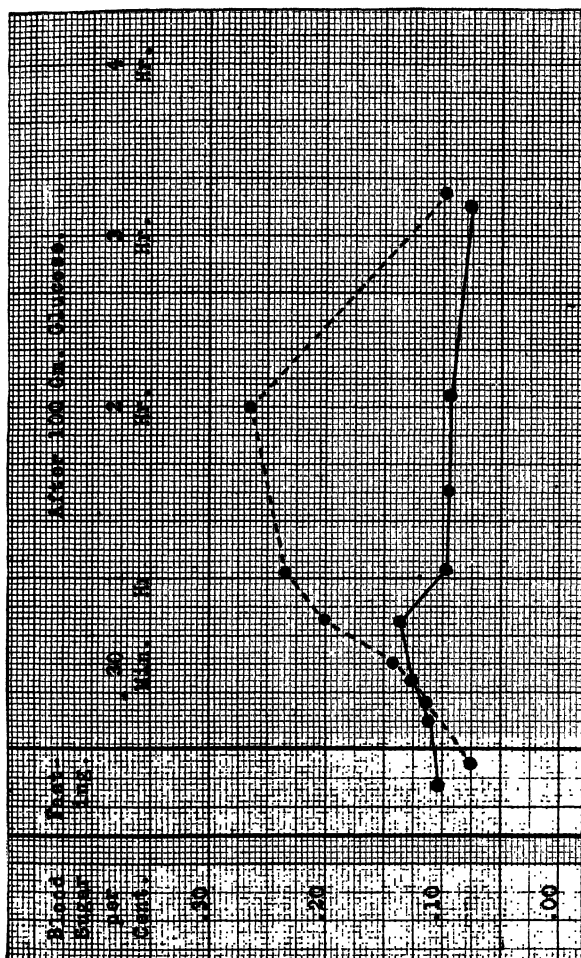


FIG. 1.—CHART SHOWING CONTRAST BETWEEN THE BLOOD-SUGAR CURVE IN A NORMAL INDIVIDUAL (continuous line) AND THAT OF A DIABETIC (broken line).

The blood-sugar curve in the diabetic is much prolonged and rises to a higher level.

nephritis, arteriosclerosis, hypertension, syphilis and gastro-intestinal carcinoma. These findings must be taken into consideration when the reaction is resorted to as a diagnostic measure.

There are other essential facts regarding the blood sugar that will be taken up a little later on.

**Glycosuria.**—RENAL (DIABETES) GLYCOSURIA; THE RELATION OF THE KIDNEY TO THE BLOOD SUGAR.—The normal urine contains traces of glucose. These are so slight that they escape the ordinary laboratory tests and thus the statement that the normal urine is free from sugar is justified from the clinical point of view.

Ordinarily sugar does not appear in the urine until the blood sugar has become considerably increased. Hamman and Hirschman believe that the renal threshold for glucose is .17 to .18 per cent. of glucose in the blood. Like all normal criteria, such as those for hemoglobin, urine volume, the size of the heart, etc., this figure is subject to some variation. However, further experience has convinced us that this percentage is correct for the average individual.

There are several points in regard to the renal threshold for glucose whose importance will be thoroughly appreciated when the relation of the blood sugar to therapy is taken up. The permeability of the kidney to the glucose of the blood is not fixed, but often varies considerably within comparatively brief periods. This may be readily appreciated from the accompanying table, which gives data from a case in which the urine contained no glucose while the blood sugar was as high as 0.237 per cent., whereas, some time later, sugar was excreted with a glycemia of 0.180 per cent. or less.

TABLE 1

DATA DEMONSTRATING THE VARIABILITY OF THE RENAL THRESHOLD TO GLUCOSE IN A CASE OF DIABETES MELLITUS

Time	Blood Sugar (Per Cent.)	Urine		
		c.c.	Glucose	
			Per Cent.	Gms.
Nov. 11. . . . .	.237	24-hour specimen.	0	0
12. . . . .	.220	24-hour specimen.	0	0
13. . . . .	.180	24-hour specimen.	0	0
Dec. 1.—11:00 a. m. . . . .	.177	.....	.....	.....
12:19 p. m. . . . .	.180	.....	.....	.....
10:45 a. m. to 12:27 p. m. . . . .	.....	70	.36	.25
3:35 p. m. . . . .	.161	.....	.....	.....
4:46 p. m. . . . .	.181	.....	.....	.....
3:36 p. m. to 4:48 p. m. . . . .	.....	98	.40	.38
Dec. 8.— 9:30 a. m. . . . .	.173	.....	.....	.....
10:25 a. m. . . . .	.142	.....	.....	.....
9:33 a. m. to 10:27 a. m. . . . .	.....	.....	+	+
11:30 a. m. . . . .	.180	.....	.....	.....
10:27 a. m. to 11:32 a. m. . . . .	.....	.....	+	+

It is often assumed that when sugar does not appear in the urine, though the level of glucose in the blood surpasses the normal renal threshold of about 0.17 per cent., the reason for this is to be sought in the presence of a nephritis. This is not the case and it must be recognized that such an impermeability of the kidney is often brought about by factors other than nephritis, concerning which little is known. The following illustrates this and serves to show as well how high the blood sugar may rise in some instances without resulting in a glycosuria.

TABLE 2

DIABETICS, SHOWING A BLOOD SUGAR OF .20 PER CENT. OR HIGHER, WHILE THE URINE WAS FREE FROM SUGAR

Blood Sugar, Per Cent.					Blood Sugar, Per Cent.				
Case 1.....	.20	...	...	...	*Case 9.....	.22	...	...	...
Case 2.....	.20	.20	...	...	Case 10.....	.24	.22	...	...
Case 3.....	.20	...	...	...	Case 11.....	.25	.21	...	...
*Case 4.....	.20	...	...	...	*Case 12.....	.25	...	...	...
Case 5.....	.20	...	...	...	Case 13.....	.27	...	...	...
Case 6.....	.21	.20	.20	...	Case 14.....	.28	.20	...	...
Case 7.....	.21	...	...	...	*Case 15.....	.31	.27	.25	...
*Case 8.....	.21	...	...	...	Case 16.....	.32	.30	.21	.20

In fact, some cases with nephritis exhibit a distinctly subnormal renal threshold to glucose. From the appended table it is readily seen that this patient put out sugar in his urine while the glucose in the blood varied between 0.10 and 0.07 per cent. This man was suffering with a considerable degree of renal involvement, as shown by the presence of albumin and a few hyaline and coarsely granular casts in the urine, a tendency to a fixation of the urinary specific gravity at a low level; a phenolsulphonephthalein excretion of 22 per cent. in 2 hours, a blood urea nitrogen of 35 mgm. per 100 c.c., and an Ambard's coefficient of urea excretion of 0.17.

TABLE 3

BLOOD-SUGAR DETERMINATIONS AND DEGREE OF GLYCOSURIA AFTER 100 GRAMS OF GLUCOSE IN A CASE OF NEPHRITIS WITH A LOWERED RENAL THRESHOLD

	Fast-ing	After 100 Grams of Glucose							
		15 min.	30 min.	45 min.	1 hour	1 hr. 30 min.	2 hrs.	3 hrs.	4 hrs.
Blood Sugar, Per Cent.....	.10	.15	.18	.23	.26	.26	.23	.10	.07
Urine Glucose, Per Cent....	.13	.13	.37	.80	1.61	3.33	2.00	1.11	.33

There is a distinct lowering of the kidney threshold for glucose, and a marked exaggeration of the blood-sugar curves both as regards the level to which it rises and the duration of the hyperglycemia. This, therefore, is a case of renal glycosuria, associated with chronic nephritis (see clinical data) and possibly diabetes mellitus as well.

The table reveals a blood-sugar curve after the administration of 100 grams of glucose which is characteristic of diabetes mellitus, or possibly of nephritis, but not of a normal person. Besides illustrating the possible hyperpermeability to glucose in nephritis, these findings furnish an instance in which the blood-sugar curve after 100 grams of glucose is not final in deciding whether a true diabetes mellitus is present or not. It has been found that certain cases of diabetes have at times at least a subnormal threshold to the blood sugar.

The fact that a condition known as "renal diabetes" or, better, "renal glycosuria" exists is constantly becoming more firmly established. Under this term is understood a glycosuria which is the result of an abnormal permeability of the kidney to sugar. The kidney in this pathological state allows a small amount of sugar to escape constantly in the urine, while the blood sugar maintains a normal level of between 0.06 and 0.11 per cent. The body has lost none of its

\* These gave clinical evidences of nephritis; the remainder did not.

power to utilize carbohydrate, and hyperglycemia is not found as it is in true diabetes mellitus. Consequently, an increase or decrease of the carbohydrate constituents of the diet has little effect on the percentage of sugar in the blood or the quantity excreted in the urine. These cases have none of the clinical manifestations of diabetes mellitus, due either to a diminished ability of the body to utilize glucose or to the presence of a hyperglycemia; there is no polydipsia, polyphagia or polyuria, no loss of weight or weakness, no pruritus or furunculosis, nor any other symptom of the disease. According to the present conception of this condition, it remains stationary, the glycosuria showing no tendency to increase, nor does diabetes mellitus develop from it; the subject continues in good health and without any abnormal symptoms or signs except a constant low-grade glycosuria. The data necessary for the diagnosis of renal diabetes are very few in number but sharply defined:

1. A glycosuria, maintained at a fairly constant level and not markedly affected by changes in the carbohydrate content of the food.
2. A normal percentage of blood sugar while the urine contains glucose.

From this description it is evident that the term "renal diabetes" is a misnomer and that "renal glycosuria" would be more appropriate.

The depression of the renal barrier to glucose and the normal blood-sugar curve, indicating no change characteristic of diabetes in the carbohydrate metabolism, in a case of this kind, are readily appreciated from the appended table.

TABLE 4

BLOOD-SUGAR DETERMINATIONS AND DEGREE OF GLYCOSURIA AFTER 100 GRAMS OF DEXTROSE IN A CASE OF RENAL GLYCOSURIA

	Fast- ing	After 100 Grams Glucose					
		35 min.	1 hr. 10 min.	1 hr. 35 min.	2 hrs. 5 min.	2 hrs. 40 min.	3 hrs. 15 min.
Blood Sugar, Per Cent.....	0.09	0.15	0.12	0.12	0.09	0.07	0.06
Urine Glucose, Per Cent.....	....	....	1.0	....	....	....	0.6

These cases require no treatment. They should, however, be very carefully watched as up to the present we are not absolutely certain that a renal glycosuria is an interesting anomaly, which is of no importance to the organism as a whole. Some of these patients have been observed over a number of years and have apparently remained in good health in spite of the persistent glycosuria.

OTHER GLYCOSURIAS; THE RELATION OF THE ENDOCRINE GLANDS TO CARBOHYDRATE METABOLISM.—The liver can convert only a limited amount of glucose to glycogen within a given time. If this quantity is exceeded, the surplus passes through the liver, enters the general circulation, and results in an increase in the blood sugar, or a hyperglycemia. When the level of the glucose in the blood rises to 0.17 per cent, or higher, some of it passes into the urine and a glycosuria can be demonstrated. This phenomenon is spoken of as *alimentary glycosuria*. Starch may be eaten in any quantity desired and will never result in the appearance of sugar in the urine. This is due to the fact that the starch is digested slowly and only comparatively small amounts of glucose derived from it pass to the liver through the portal circulation at any one time. When sugars are taken in any quantity, they are ab-

sorbed much more rapidly, as they require less digestive preparation, and alimentary glycosuria may result. Von Noorden has designated the following as the limits of tolerance of normal persons. It should be borne in mind that the susceptibility of different persons varies much in this regard.

Lactose .....	120 grams
Saccharose .....	150-200 grams
Levulose .....	120-150 grams
Glucose .....	150-180 grams
Galactose .....	20 grams

Claude Bernard discovered that puncture of the floor of the fourth ventricle in the region of the apex of the calamus scriptorius, a procedure known as "*piqûre*," resulted in glycosuria for several hours. This is effective only when the liver contains glycogen and hence must be regarded as a process in which there is a more rapid mobilization of glucose from glycogen than occurs under normal circumstances. It is essentially different from diabetes mellitus, in which the hyperglycemia is brought about by the inability of the tissues to utilize the glucose in the blood.

The impulses set up by *piqûre* pass through the cervical nerves to the thoracic sympathetic system, and thence by way of the splanchnic nerves to the hepatic plexus. An interruption of any part of this nervous path renders *piqûre* ineffective. A further very interesting fact that has been developed in this connection is that the procedure is not active if the adrenals have been removed. This correlates glycosuria produced by the subcutaneous injection of *epinephrin* closely with the nervous system.

There is abundant evidence in the literature that *emotional stimuli* may give rise to temporary glycosurias in many instances, and a few cases of diabetes mellitus have been reported whose onset is supposed to have coincided with a psychic crisis. Cannon and Fiske found sugar in twelve members of a foot-ball squad of twenty-five after the final and most exciting contest of the season. Five of the positive cases were among substitutes who did not participate in the game. A spectator of the contest whose urine was examined also, had a marked glycosuria which disappeared on the next day. Folin, Denis and Smilie demonstrated sugar in the urine of about 17 per cent. of seventy students directly after an important examination. Cannon believes that an increased secretion of the adrenal glands brought on by emotion is an essential factor in the causation of these temporary glycosurias.

In diabetes mellitus it is now generally appreciated that *mental stress* and strain is a potent influence in increasing the glycosuria and diminishing the carbohydrate tolerance. This will be taken up in detail under Treatment. It has been known for some time that severe trauma, especially about the head, may result in the appearance of sugar in the urine. With the appreciation we now have of the probable mechanism of the production of hyperglycemia and glycosuria of *piqûre* and increased secretion of *epinephrin* by mobilization of glucose from the glycogen of the liver, we do not believe that true diabetes, in which the power of the body to utilize glucose is diminished, is produced by emotional strain or nervous shock. D. S. Lewis, who had been at a base hospital in France for two years, informed the author that in that time he had seen only two cases of diabetes. This is fairly good evidence that



even the terrific strain imposed by the recent war is not often productive of diabetes. A man with a low carbohydrate tolerance, with what may be considered a latent diabetes, may have his disease brought to the fore and his carbohydrate metabolism permanently injured by emotional stress and an excessive secretion of epinephrin. This is in all probability the way in which such cases of diabetes mellitus are brought about.

Overactivity of the *pars nervosa*, the posterior lobe of the *hypophysis*, will result in a diminished tolerance for carbohydrates and glycosuria. This gland, apparently, as well as the adrenal, is necessary to allow *pituitary* to be active. Its mode of action is therefore the same as that described for Claude Bernard's puncture. Exactly what rôle the *hypophysis* plays in this connection is not definitely established. From the clinical point of view it is known that cases of hyperpituitarism exhibit a lowered carbohydrate tolerance and are prone to have a glycosuria while the the gland is overactive.

*Hyperthyroidism* is, according to Geyelin, responsible for a hyperglycemia in the moderate and severe types of this disease in about 90 per cent. of the cases. Glycosuria, either spontaneous or alimentary, was found to be an equally constant symptom. Blood-sugar curves resembling those in diabetes after the ingestion of 100 grams of glucose were demonstrated by Hamman and Hirschman. This anomaly had a tendency to disappear after a part of the thyroid gland had been extirpated. In some cases of diabetes, signs of exophthalmic goiter are undoubtedly present; the presence of severe diabetes, however, is extremely uncommon. In myxedema, the tolerance for carbohydrates is increased.

The *parathyroid glands* are supposed to have an influence on the utilization of glucose, exactly opposed to that of the thyroid. Oversecretion increases carbohydrate tolerance and vice versa. These glands have not as yet been found to have any bearing on the clinical aspect of glycosuria. The relation of the pancreas to diabetes will be discussed under Etiology.

The subject of the relation of the endocrine glands to diabetes has furnished a very tempting field for theorization. If only the proved facts are considered, it is very apparent that our knowledge is based on very scant evidence and that enthusiasm should not carry us beyond the bounds of reason. Nearly all the endocrine glands have at one time or another been supposed to have some relation to diabetes mellitus. At present it is believed that, excepting the pancreas, the disturbances of these organs may cause a derangement of carbohydrate metabolism resulting in a glycosuria, which, however, is not necessarily synonymous with diabetes.

**The Diagnosis of Diabetes Mellitus.**—The diagnosis of diabetes mellitus depends principally upon the demonstration of glucose in the urine. If this is not constantly present, or shows atypical results after suitable diets have been instituted, a glucose tolerance test, as judged both by the blood and urine, must be resorted to. The possibility of endocrine disturbances and a kidney hyperpermeable to dextrose must be kept in mind as producing a glycosuria, which is to be distinguished from true diabetes. However, it is much the safest rule to treat every case of glycosuria as one of diabetes until there is definite proof to the contrary.

**THE IDENTIFICATION OF GLUCOSE IN THE URINE.**—Fehling's solution or one of its modifications is deservedly the most popular test. About 5 c.c. of these solutions in a test-tube is ample to carry out this procedure. The common practice of filling a test-tube half or three-quarters full with the copper solutions is not only a waste of chemicals but makes the carrying out of the test much more difficult because of spattering and the results are much harder to interpret since the color changes are apt to be less pronounced. When the reduction is very marked, there is usually no doubt that glucose is present. There is a host of substances, lactose, pentose, levulose, maltose, glycuronic acid, creatinin, uric acid, albumin, urea and others which, especially in concentrated urines, is likely to produce a suggestive color. In these instances, further tests must be carried out if the reducing substance is to be identified as glucose.

*Fehling's Solution.*—Two solutions are required:

I. 34.65 grams of copper sulphate are dissolved in water and made up to 500 c.c.

II. 125 grams of potassium hydroxid and 173 grams of Rochelle salts (potassium and sodium tartrate) are dissolved in water and made up to 500 c.c.

These solutions must be kept separately. If mixed they deteriorate rapidly. A mixture of equal parts of I and II are used to perform Fehling's test. About 1 c.c. of this mixture is diluted with 3 or 4 c.c. of water in a test-tube. This is boiled (in order to determine whether there is any reducing substance present) and if no red color forms, 5 to 15 drops of urine are added and boiled again. If the urine becomes yellowish or red, glucose or some other reducing substance is present.

This test, since it requires two solutions instead of one, and yields greenish-yellow colors that are confusing with very many substances that do not affect the copper in the modification to be detailed, has been largely discarded in its favor.

*Benedict's Modification of Fehling's Solution.\**—This solution has the following composition:

	grams or c.c.
Copper sulphate (pure crystallized).....	17.3
Sodium or potassium citrate.....	173.0
Sodium carbonate (crystallized)*.....	200.0
Distilled water to make.....	1,000.0
The citrate and carbonate are dissolved together (with the aid of heat) in about 700 c.c. of water. The mixture is then poured (through a filter, if necessary) into a larger breaker or casserole. The copper sulphate (which should be dissolved separately in about 100 c.c. of water) is then poured slowly into the first solution, with constant stirring. The mixture is then cooled and diluted to one liter.	

\* One-half the weight of the anhydrous salt may be used.

This reagent is about ten times as sensitive to sugar in urine as is Fehling's or Haines' solution and, unlike these latter solutions, is not appreciably reduced by creatinin, uric acid, chloroform or the simple aldehyds. The mixture may be kept indefinitely in uncolored glass or cork-stoppered bottles.

For the detection of glucose in urine, about 5 c.c. of the reagent are placed in a test-tube and 8 to 10 drops (not more) of the urine to be

\* Benedict, S. B., Jour. Am. Med. Ass'n, 1911, lvii, 1193.

examined are added. The mixture is then heated to vigorous boiling, kept at this temperature for one or two minutes, and allowed to cool spontaneously. In the presence of glucose *the entire body of the solution will be filled with a precipitate*, which may be red, yellow or greenish in tinge. If the quantity of glucose is low (under 0.3 per cent.) the precipitate forms only on cooling.

If any doubt exists in the examiner's mind as to whether a given reducing substance is glucose or not, two additional qualitative tests may be made—the phenylhydrazin test and the fermentation test—and if both are positive they indicate that a glycosuria is present.

**Phenylhydrazin Test.**—Kowarsky's method as described by F. C. Wood is easily performed. Five drops of phenylhydrazin are mixed in a test-tube with 10 drops of glacial acetic acid and 1 c.c. of a saturated solution of sodium chlorid. A curdy mass is formed of phenylhydrazin hydrochlorid and sodium acetate. Then add 2 to 3 c.c. of the urine to be tested and heat for at least 2 minutes over a flame. If over 0.5 per cent. of glucose is present, the glucosazone crystals form immediately. If smaller amounts are present, the test-tube should be allowed to cool for a few minutes. The crystals which have collected at the bottom are removed with a pipet and examined under the microscope with a one-fifth objective. The crystals are long, fine, yellow needles arranged in sheaves and spherical masses.

**Fermentation Test.**—The urine is thoroughly mixed with a small quantity of yeast. (If possible, it is best to boil the urine first. This destroys the amylase of the urine and thus prevents the formation of gas from the starch present in the usual commercial yeast.) It is placed in a fermentation tube and put into an incubator or a warm place for several hours or over night. The presence of gas indicates glucose. It is necessary to perform a control test with urine known to be free from sugar, as different samples of yeast vary much in regard to the amount of gas for which they may be responsible without the aid of dextrose.

When all three tests are distinctly positive, there is no doubt that glucose is present. But if the tests are not clear-cut, or even if they are negative, it cannot be considered certain that small amounts of glucose are absent. It is almost absurd how difficult this problem of determining the presence or absence of traces of glucose in the urine may become, and yet it is often of the utmost importance to know whether an individual should be considered normal or regarded as a very mild case of diabetes. In such instances, the glucose tolerance test must be resorted to. (For the identification of pentose, lactose, etc., the reader is referred to special works on the subject.)

**TEST FOR CARBOHYDRATE TOLERANCE.**—Glucose is the sugar most frequently used to test the tolerance of an individual. The method of giving 100 grams of this substance on an empty stomach has already been detailed under blood sugar. At the present time, the resulting blood-sugar curve is considered to be of greater significance than the appearance or absence of glucose in the urine. It is a generally accepted fact to-day that there should be no glycosuria whatsoever evident in a normal individual after taking 100 grams of glucose. If glucose appears in the urine, it is most frequently found during the first two or three hours after the sugar has been taken. The reason for this is very evident when the blood-sugar curves are taken into consideration. It is during this period that the blood sugar reaches its

highest level and is most likely to pass through the kidney. Hence, in carrying out such a test for sugar tolerance, the urine is usually collected in two periods, one covering the first two hours after the glucose is taken, the other covering the remainder of the twenty-four hours. A trace of sugar in the first specimen was formerly considered to be within normal range; however, more recent investigations have indicated that even this should be regarded with suspicion; the presence of dextrose in the second period may be regarded as undoubted evidence of a diminished tolerance for glucose. The details of interpreting the blood-sugar curve have been given under blood sugar. It should be recognized that by means of a few blood-sugar determinations, a very vexatious diagnostic problem may frequently be answered very rapidly and with comparatively little effort.

**Acidosis.**—CHEMISTRY OF ACIDOSIS.—Acidosis is a term which signifies that there is an accumulation of acids within the body. Such an abnormal retention brings about certain changes which are of vital importance to the organism. The term acidosis must be used carefully; the formation or excretion of an amount of acid substances in excess of the normal is not synonymous with it; there must be a retention of acids before their effect becomes manifest and before we can designate such a symptom-complex as acidosis.

There are various acids which may be responsible for acidosis. Those that are associated with this condition in uremia, myocardial insufficiency, the diarrheas, etc., have not been satisfactorily determined. We are best informed concerning those that are the cause of diabetic acidosis. These are frequently, in a rather loose way, spoken of as the acid substances, the acid bodies, or the acetone bodies. These are:

1. Beta-oxybutyric acid .....  $\text{CH}_3\text{CHOHCH}_2\text{COOH}$

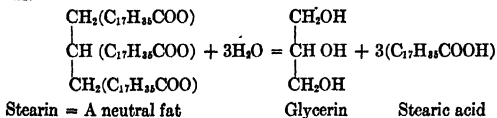
2. Diacetic acid .....  $\text{CH}_3\text{COCH}_2\text{COOH}$

and derived from 1 and 2

3. Acetone .....  $\text{CH}_3\text{COCH}_3$ .

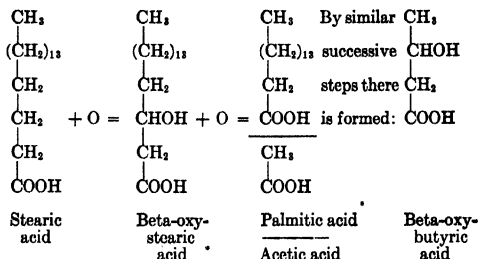
Acetone was discovered in diabetic urine by Peters (1857), diacetic acid by Gerhardt (1865), and recognized as such by Tollens (1881). Beta-oxybutyric acid, the most important of these substances, was demonstrated by Stadelman, by Minkowski and by Kulz (1883). At first, carbohydrate was regarded as the mother substance of these abnormal urinary constituents. The error of this conception soon became evident, and the proteins and fats were in turn made responsible for the appearance of the acids in diabetic urines. At present, it is known that carbohydrates and alcohol do not give rise to beta-oxybutyric acid and its derivatives, but that both fats and proteins may do so.

Normally, beta-oxybutyric acid is formed in the digestion of both fats and proteins. The neutral fats are changed to fatty acid and glycerin.



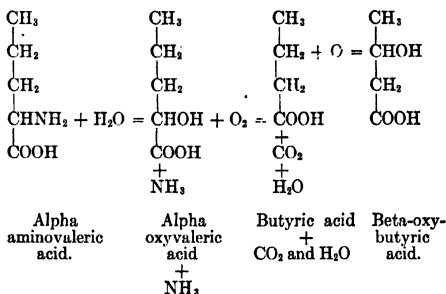
The fatty acid—stearic acid, in this instance—becomes oxidized by changes which always occur at a definite point in the chain of carbon

atoms of which it is made up; this is the third, or beta-carbon atom, thus:



In this manner there is first formed a beta-oxy-acid and subsequently two carbon atoms are split off and the main part of the original molecule now constitutes a fatty acid having two less carbon atoms in its chains than at first. It can be readily appreciated how this chemical process continues until beta-oxybutyric acid is produced.

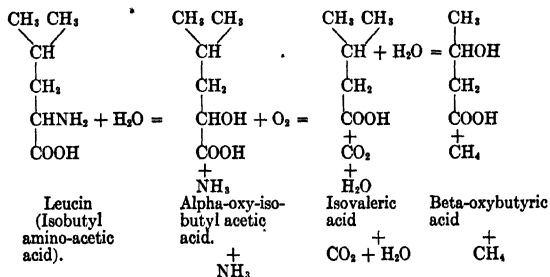
It becomes evident that only those fatty acids with an even number of carbon atoms will be changed to beta-oxybutyric acid; those with an uneven number would give rise to propionic acid,  $\text{CH}_3\text{CH}_2\text{COOH}$ , with three carbon atoms. Ringer and others have shown that the latter acid is changed to glucose and not to acid substances in the diabetic animal. From the practical point of view, we need not concern ourselves with the latter fact, as the fat of our food is composed exclusively of fats whose fatty acids contain an even number of carbon atoms. The attempt to produce fats that would give rise to glucose instead of beta-oxybutyric acid has resulted in the marketing of "Intarvin" (glycerol margarate). This preparation may serve a useful purpose if it is desired to feed fats in the presence of an acidosis; its real value is as yet a matter for determination.



The derivation of beta-oxybutyric acid from proteins is brought about by a process which resembles in many respects that noted for the fats. The proteins before absorption are broken up into their constituent amino-acids. In the amino-acids, the number of carbon atoms in the chain necessary to form beta-oxybutyric acid is an odd one and

not an even figure as in the fatty acids. This is due to the fact that the initial process, which rids the amino-acid of its nitrogen (deamination) occurs at the alpha carbon atom, which always carries the  $\text{NH}_2$  group. In this manner, the number of carbon atoms in the chain is brought from an uneven to an even one. The subsequent oxidative processes then follow the laws laid down for the fatty acids. The simplest chemical change of this type is that occurring in aminovaleric acid, as above.

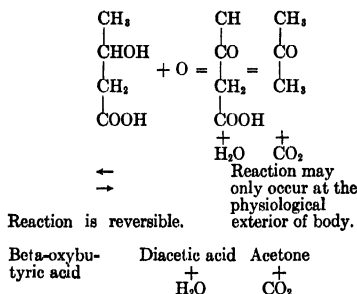
The more complex branched amino-acids may also yield beta-oxybutyric acid by replacement of one of the branched groups by oxidation. This may be demonstrated by the reactions which leucin undergoes.



The amino-acids which yield propionic acid and not butyric acid give rise to glucose. It has already been mentioned how 58 per cent. of protein may be changed to sugar within the body. According to Magnus-Levy, the maximal amount of beta-oxybutyric acid which can be derived from fat is 36.2 per cent. The caloric value of 1 gram of beta-oxybutyric acid is estimated at 4.5 calories. The caloric loss to the diabetic may therefore be fairly large in this regard. The fate of beta-oxybutyric acid in the normal person is that it becomes changed to carbon dioxid and water— $\text{CH}_3\text{CHOHCH}_2\text{COOH} = 4\text{CO}_2 + 4\text{H}_2\text{O}$ . In the diabetic individual who has lost the power to oxidize beta-oxybutyric acid along normal paths, much of this acid remains unchanged, while a portion of it becomes diacetic acid. The diacetic acid in turn may in part give rise to acetone. Embden and Folin have both claimed that acetone is produced only at the physiological exterior of the body in the lungs and in the urine. In any case the determination of acetone would only have the significance that could be attributed to diacetic acid. The reaction by which diacetic acid is derived from oxybutyric acid is in large part a reversible one; that is, either substance may give rise to the other. In this instance again the significance of either of these substances, as determined in the blood or urine, may be given an identical interpretation. From the clinical point of view, therefore, the significance of all the acid bodies may be regarded as similar. The chemical changes which beta-oxybutyric acid may undergo in the diabetic are shown on the opposite page.

The reason why in some individuals beta-oxybutyric acid is not oxidized in a normal manner is to be found in the lack of the proper utilization of carbohydrate. This is only an empirical and in reality no adequate answer to our question. One observer epitomized the situ-

ation when he wrote that the acid bodies burn in the fire of the carbohydrates. When the carbohydrate intake is less than about 50 grams



the acid substances appear in the urine. This is true for many conditions, toxemia of pregnancy, excessive vomiting, carcinoma, fever, starvation, etc. In advanced cases of diabetes there is the most complete form of carbohydrate starvation known in medicine. Not only may the glucose derived from carbohydrate be excreted in the urine and thus remain unutilized, but that derived from the protein may have the same fate. It is only natural that under these circumstances the most marked degree of acidosis, brought on by the acetone bodies, occurs in this disease.

The observations of Zeller in 1914 first suggested that there was a closer relation of the amount of B. oxybutyric acid oxidized to the consumption of carbohydrate than had been supposed. He found that the appearance of acetone in the urine was dependent not only on the absence of carbohydrate in the food but that the quantity of fat also played a rôle. When one molecule of sugar was present to two of fat then acetone was found in the urine. It remained for Shaffer and Woodyatt to formulate these facts more precisely and put them upon what may be regarded as a mathematical basis by which the proper proportions of protein, fat and carbohydrate in the dietary of the diabetic may be prescribed.

The various foods on utilization in the body yield two products, glucose and fatty acids. These have the same effect upon the organism regardless of whether they are derived from protein, fat or carbohydrate. Hence a knowledge of the potential value of any diet in fatty acid and glucose is the all-important factor in regulating an acidosis. The following equations are, in round numbers the figures that are generally accepted. It is useless to attempt to deal in fractions or quarrel about the finer points in such a table, for there are many influences that render it of approximate accuracy only, although it is none the less important on this account. The most evident reason why the scheme is not 100 per cent. accurate is that the consumption of a certain amount of food does not necessarily imply that this is the quantity utilized by the body; the organism may draw upon its own tissues and oxidize a greater volume than it has ingested, or it may consume less and store some of it for future use as protein, glycogen or fat. Even allowing for these eventualities, the calculation of the fatty acid: glucose ratio of the diet furnishes

us with the most reliable guide for the proper dietary regulation with which to control acidosis in the diabetic patient.

100 grams protein	yield 46 grams fatty acid	58 grams glucose
100 grams fat	yield 90 grams fatty acid	10 grams glucose
100 grams carbohydrate	yield 0 grams fatty acid	100 grams glucose

The thorough understanding of the above table has cleared up many facts that were considered inexplicable. For instance, it has shown us how the various starch cures—especially the oatmeal cure—acted in rendering a urine free from sugar; a diet containing much starch may or may not yield as much glucose to the body as one that is high in protein and low in carbohydrate; the explanation is exceedingly simple.

On a basis of this equation one can also calculate a diet which should furnish no more B. oxybutyric acid than the patient may consume. The fatty acid: glucose ratio (or F.A.: G., as it may be expressed briefly) required so that there shall be no unchanged residue of B. oxybutyric acid should not exceed a certain figure. According to some authors the F.A.: G. ratio may be 3:1, according to others 2:1 and according to still others 1.5:1. A very safe rule, and one which provides a thoroughly adequate amount of fat in the diet, is to allow a ratio of about 1.2:1, and to increase or diminish it as circumstances demand. Thus one of the diets, to be detailed under treatment, contains protein 75 grams, fat 175 grams and carbohydrate 100 grams. On analysis for the F.A.: G. ratio we obtain the following:

		<i>Fatty Acid</i>	<i>Glucose</i>
Protein .....	75 grams =	34.5	43.5
Fat .....	175 grams =	157.5	17.5
Carbohydrate .....	100 grams =		100.0
		<hr/>	<hr/>
		192.0	161.0
F.A.: G. = $\frac{192.0}{161.0}$ = 1.2:1			

The proportion of fatty acid to glucose in this diet therefore is satisfactory and need not be considered as one likely to bring about an acidosis. To any one following this procedure in prescribing accurate diets it soon becomes apparent that the F.A.: G. that is successful in preventing the appearance of acetone in the urine varies much not only in different patients but in the same patient from time to time. Thus we have found traces of acetone in the urine when the F.A.: G. was 0.74 and missed it with a ratio of 3:1. Another fact worth remembering is that traces of acetone and diacetic acid, even considerable traces, are likely to disappear although the patient's diet is not changed in any way. Von Noorden pointed this out many years ago and it has proved to be correct. It is as though the function to utilize fatty acids will improve under certain conditions just as the carbohydrate tolerance of the diabetic will often increase if it is given an opportunity. Taking the general consensus of opinion and experience into consideration it is very evident that the diabetic has a much greater reserve to meet emergencies if there is no acetonuria than when it is present; the existence of traces of acetonuria do no harm for the moment. The control of diet by the mathematical scheme explained above has been a very great advance in the proper management of glycosuria and particularly acetonuria and acidosis.

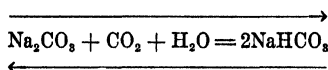


When acids are retained within the organism, accumulating in the blood and tissues, the symptom-complex of acidosis results. There are certain compensatory processes which tend to neutralize the acids; when the acids finally predominate, death from diabetic coma is the outcome.

The kidneys are the main agency by which the non-volatile acids, such as those of the beta-oxybutyric group, are excreted. The acid in the blood does not pass into the urine as an acid but as a salt. There is a small amount of fixed alkali to form such salts. When this is exhausted, the ammonia, which ordinarily is synthesized to urea, aids in the neutralizing process and thus permits an increased quantity of acid substances to be eliminated by the kidneys. The maximum amount of acid bodies which may be excreted in this way, without the aid of any medication, has been computed to be approximately 30 grams. If the production of acids exceeds the output, the excess remains within the body until it can combine with a base. Such a base may be supplied by the giving of alkalis, usually bicarbonate of soda. When large amounts of this salt were given, Magnus-Levy and Joslin both demonstrated cases in which approximately 150 grams of acid substances were excreted in 24 hours.

The alkalis of the body are necessary to carry out the internal respiration. They transport the carbon dioxide from the tissues to the lungs, and then return to repeat the process. This may be illustrated by the following equation, which shows what reactions may take place when sodium carbonate performs this function.

*In the tissues:* Sodium carbonate combines with carbon dioxide and water to form sodium bicarbonate, and is then carried to the lungs, where:



*In the lungs:* The bicarbonate of soda gives up the carbon dioxide and water and returns to the tissues as sodium carbonate by way of the blood stream to repeat the process.

It is perfectly obvious under these circumstances that if beta-oxybutyric or diacetic acid combine with the sodium carbonate, internal respiration cannot proceed at the same rate, and in consequence, the tension of the carbon dioxide in the blood, and also in the alveolar air, in which the tension is the same as in the blood, becomes lowered. Another graphic way of expressing these facts is by a diagram which Peabody suggested. (Fig. 2.)

**DEGREE OF ACIDOSIS.**—The criteria by which the intensity of an acidosis may be judged are very numerous. They will all be mentioned; only a few of them need be restored to in the management of diabetes.

1. *The Reaction of the Urine.*—If this is neutral or alkaline, it may be assumed that the acid substances are not exhausting the body's supply of alkali and that there is an abundant supply of the latter to neutralize any acid. This test has only a limited application, as the urine may be acid, even after the administration of considerable amounts of bicarbonate of soda, and yet there may be no danger from acidosis.

2. *The Presence of Acetone Substances in the Urine.*—There are usually found for a period of months or years before dangerous symptoms develop. Occasional cases have been reported in which diabetic coma has supervened, though the reactions for acid bodies in the urine were slight or absent. These instances are extremely uncommon; the author has seen it only once.

(a) *Qualitative tests for acetone and diacetic acid* are very helpful. They may be recorded according to the intensity of the color which they yield, as +, ++, +++, or +++++. Such crude attempts at quantitative estimation are very time saving, as there is generally no need to resort to the more complicated tests for acidosis until the reactions have become at least fairly intense.

*Legal's test for acetone* may be easily performed by putting 5–10 c.c. of urine in a test-tube, adding a little strong sodium or potassium hydroxid solution and a few drops of a solution of sodium nitroprussid; a

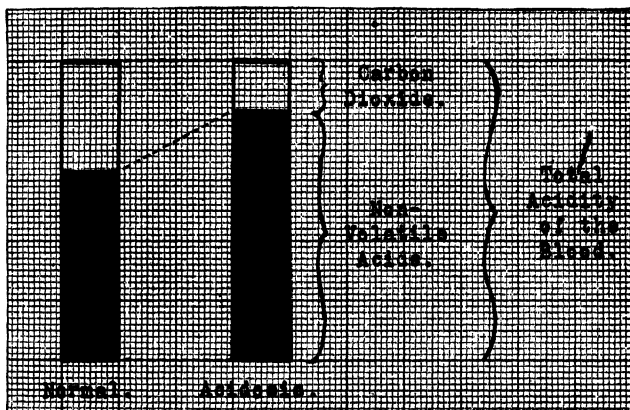


FIG. 2.—CHART SHOWING INCREASE IN NON-VOLATILE ACID AND CORRESPONDING DECREASE OF CARBON DIOXID IN ACIDOSIS, AS COMPARED TO NORMAL BLOOD.

thin layer of this mixture is poured on a flat white porcelain dish and a few drops of glacial acetic acid added; if acetone is present a purple color results where the glacial acetic acid comes in contact with the fluid; the depth of the purple color is in direct proportion to the amount of acetone in the urine.

*Gerhardt's ferric chlorid test for diacetic acid* is exceedingly simple: To 5–10 c.c. of urine in a test-tube, a 10-per cent. or stronger solution of ferric chlorid is added; the addition should be made slowly; at first a white precipitate of phosphates is formed; more ferric chlorid should be added until this dissolves, when the resultant color may be noted. A mahogany red indicates the presence of diacetic acid. Here again, the intensity of the color is of some value, as indicating the amount of this acid. If the patient has been taking salicylates in any form, cyanates or acetates, this test may be positive. If the color present is due to diacetic acid, then Legal's test should be positive as

well; if it is not, the acetone test is also negative. If the urine, giving a reddish-brown color with ferric chlorid, is boiled for two minutes, the reaction will disappear if it is due to diacetic acid, as this substance readily volatilizes; whereas, if it persists, it is due to some other substance.

(b) The *quantitative estimations* of the acetone substances in the urine are difficult and tedious. Furthermore, from the clinician's point of view, it is not so much the quantity of these materials which are excreted that is of significance, but the amount which is retained, and the effect which they have on the body. For these reasons, these laboratory tests have been largely discontinued except for scientific purposes. Mention has previously been made of the fact that only about 30 grams of acid substances measured as beta-oxybutyric acid will be excreted in a day, unless alkali is given as well, and then the amount has been observed to rise as high as 150 grams.

3. *Quantitative Estimation of Urinary Ammonia*.—This is one of the most significant criteria of the intensity of an acidosis. To-day, it has been largely replaced in the clinic by the determination of the carbon dioxid tension of the blood. Under normal circumstances, about 0.5 gram of ammonia is excreted in the urine in 24 hours. The ammonia nitrogen thus constitutes about 5 per cent. of the total nitrogen. This percentage relation is often spoken of as the ammonia index. The acid bodies combine with ammonia and are thus excreted as salts; the amount of ammonia, therefore, furnishes an index of the quantity of acid substances that are present in the urine. Magnus-Levy has formulated these numerical relationships as follows:

<i>Urinary Ammonia in 24 Hours (Grams)</i>		<i>Beta-oxybutyric Acid (Grams)</i>
0.5 — 1.0	is normal.	
2	correspond to	6
5	" "	20
8	" "	36 — 40

These are the values for acid bodies estimated as beta-oxybutyric, provided no alkalis are administered. These would naturally raise the amounts of acid substances and diminish the ammonia. If the body is

TABLE 5  
RELATION BETWEEN ACIDOSIS, ALKALI THERAPY AND URINARY AMMONIA

Date	NH <sub>3</sub> (Grams)	Acidosis as B-oxy- butyric Acid (Grams)	Sodium Bicarbonate	
			By Mouth (Grams)	By Infusion (Grams)
Case 1.—Dec. 8. . . . .	3.9	38.3	60	10
10. . . . .	3.2	24.7	60	10
15. . . . .	3.4	16.1	0	0
17. . . . .	3.6	16.4	0	0
21. . . . .	4.0	17.7	0	0
29. . . . .	3.6	12.7	0	0
Case 2.—Dec. 2. . . . .	8.8	....	0	0
4. . . . .	2.3	60.2	120	32
7. . . . .	3.1	59.3	120	0
11. . . . .	4.1	55.2	160	0

putting out the maximum amount of ammonia of which it is capable, and in spite of this acid bodies are being retained, then alkali, whether given by mouth, infusion or rectum, will increase the excretion of

acetone substances, but will not diminish the urinary ammonia. These facts may be noted in Case 1 shown in Table 5 above. In this instance, the exhibition of considerable quantities of bicarbonate of soda caused 38.3 grams of beta-oxybutyric acid to be eliminated on the first day charted; when the alkali therapy was omitted, the beta-oxybutyric dropped to about 16 grams; the ammonia, however, remained throughout at a level of from 3.2 to 4 grams. In this case, therefore, there was no reserve alkali in the body, even when large doses of soda were given, and the patient was perilously near the border-line. In Case 2, the use of bicarbonate of soda depressed the ammonia in the urine to a considerable degree and there evidently was a margin of safety.

How the increase of ammonia is associated with a rise in the excretion of large amounts of acid bodies is apparent from the data of the case in Table 6. The rise in the elimination of the beta-oxybutyric acid in this case was brought about by the absorption of large amounts of fat.

Four to six grams of ammonia a day may be kept up in some instances for a considerable period. Higher amounts may be present, as the record of 8.8 grams in one of the previous tables shows; 10 and even 12 grams a day have been exceptionally noted by various observers. As a rule, there is no danger from acidosis if the ammonia remains at or below 2 grams in the 24 hours and the ammonia coefficient is 20 per cent. or less.

TABLE 6

INCREASE OF URINARY AMMONIA ASSOCIATED WITH A RISE IN THE EXCRETION OF BETA-OXYBUTYRIC ACID AND ITS DERIVATIVES

Date	Ammonia (Grams)	Acid Substances as B-oxybutyric Acid (Grams)
May 11.....	2.8	5.3
13.....	1.9	4.9
26.....	5.2	29.3
27.....	6.0	34.8

4. *Carbon-Dioxid Tension of the Blood and the Alveolar Air.*—The degree of acidosis may be determined by the quantitative excretion of acetone bodies in the urine and by the amount of reserve alkali they are drawing upon as outlined above. The most rational test, however, is the one which measures how far the acidosis encroaches upon the vital activities of the organism. This, as previously stated, is to be found in the carbon dioxid of the alveolar air. The carbon-dioxid tension may be measured in the blood according to Van Slyke's method or in the alveolar air by the procedure of Haldane or Fridericia. By far the simplest of all of them is the test devised by *Marriott*; it requires only such apparatus as is readily portable, and results may be obtained with no more effort than is necessary to take an ordinary blood-pressure reading. The *technic* is as follows:<sup>5</sup>

Two procedures are involved: the collection of the alveolar air and the analysis of the sample. The method of collection is essentially that of Plesch, as modified by Higgins. A rubber bag of approximately 1,500 c.c. capacity is connected by means of a short rubber tube to a glass mouthpiece. About 600 c.c. of air are blown into the bag with an atomizer bulb, and the rubber tube clamped off by a pinchcock. The subject should be at rest and breathing naturally. At the end of a normal expiration, the subject takes the tube in his mouth, the pinchcock is

released and the subject's nose closed by the observer. The subject breathes back and forth from the bag four times in twenty seconds, emptying the bag at each inspiration. The observer should indicate when to breathe in and out. Breathing more frequently will not greatly alter the results. At the end of twenty seconds the tube is clamped off and the air analyzed. The analysis should be carried out within three minutes' time, as carbon dioxid rapidly escapes through rubber.

The foregoing procedure applies only to patients who are capable of coöperating to some extent. In the case of comatose patients, the initial amount of air in the rubber bag must be greater (1,000 c.c. at least), and the period of rebreathing prolonged to 30 seconds. This is necessary, as it is not feasible that the bag be completely emptied of air at each inspiration, and therefore a longer time is required for the carbon-dioxid tension in the bag and in the lungs to become equal. The initial amount of air in the bag should be such that it is at least one-half and preferably as much as two-thirds emptied at each inspiration. Since comatose patients cannot hold the mouthpiece, some form of mask is necessary.

For *analysis of the air samples*, the apparatus required comprises eight test-tubes, containing standard phosphate solutions; a standard bicarbonate solution; a small test-tube; a glass tube or pipet drawn out to a capillary point, and a box for color comparison.

In analyzing a sample of air, about 2 or 3 c.c. of the standard bicarbonate solution are poured into a clean test-tube of the same diameter as the tubes containing standard phosphate solutions, but from 100 to 150 mm. long. Air from the bag is then blown through the solution by means of a glass tube drawn out to a fine capillary point, until the solution is saturated, as shown by the fact that no other color change occurs. The tube is stoppered and the color immediately compared with that in the standard tubes.\*

In normal individuals, the carbon-dioxid tension of the alveolar air (and of the blood) is 40 to 45 mm. of mercury. Tensions between 40 and 30 are indicative of mild degrees of acidosis; below this point, the acidosis may be considered to be severe. A figure of 20 or less occurs when there is impending coma. Readings as low as 13, 12 or 8 mm. are not uncommon. Such cases usually terminate fatally.

5. *Blood Lipids*.—The blood lipids are often markedly increased in diabetes. The observation that fat frequently occurred in the blood in such amounts as to be visible to the naked eye was made a considerable number of years ago. The exact significance of this fact is not known at the present time. It has been shown that a diet high in fat will not increase the cholesterol of the blood in diabetic individuals.

**SYMPTOMS OF ACIDOSIS.**—The symptoms of acidosis are very few; when the condition is marked, however, they are very characteristic, and when present, demand immediate relief. If steps are not taken under these circumstances to combat the acidosis, diabetic coma is almost certain to follow. As previously mentioned, the excretion of the acid substances in the urine usually precedes by months and even years the onset of the other objective and subjective clinical signs. Fatigue,

\* For the preparation of the standard solutions, etc., the reader is referred to Marriott's original article. All the apparatus necessary for the test may be purchased at Hynson, Westcott and Dunning, Baltimore.

lassitude and irritability are often forerunners of most serious symptoms. Nausea, vomiting and occasionally diarrhea are characteristic of the condition as it becomes more marked. In one case there was esophageal spasm a few days before coma set in. As the carbon-dioxid tension of the blood and alveolar air diminish, a very characteristic form of dyspnea, often spoken of as hyperpnea, sets in. The frequency of the respiration is not increased, but it is much deeper than normal. One patient characterized this symptom very well when he said that he was not short of breath, but that very deep breathing would wake him up during the night and that when he shaved in the mornings, he had to take such deep breaths that he was obliged to pause in order to obtain relief. Such deep breathing without any increase in the frequency of the respiratory movements is always a danger signal, and is a clinical symptom which usually is not sought for as diligently as it should be. If the acidosis becomes more intense, the deep breathing continues, drowsiness sets in and becomes more marked. When unconsciousness has once supervened, death usually follows within 48 hours unless insulin is administered. The use of insulin has changed the prognosis in diabetic coma entirely. With it the majority recover, whereas formerly nearly all succumbed.

**Etiology.**—According to the available vital statistics, diabetes is apparently more common to-day than it was a few years ago. This is probably due to the more frequent urinary examinations and better education of the public and physicians. The result is that a proper diagnosis is now made in the majority of instances and the causes of death are more nearly correctly reported. In 1915, the death rate per 1,000 of population from all causes in the registration of the United States was 13.5 and that for diabetes 0.175. These figures furnish distinct evidence as to the great prevalence of this disease.

**Age.**—The onset of the disease is most frequent in the fifth and sixth decades of life, though no age is exempt. Joslin has recently shown that it is not infrequent at an early age; 4.7 per cent. of his cases occurred during the first ten years of life.

**Sex.**—It is generally agreed that males are more subject to the disease. Statistics in this regard are apt to be somewhat misleading, as they will vary according to individual experiences. Thus the writer finds that in dispensaries there is a preponderance of women; the men generally will not come for treatment until they are so ill that they must enter the hospital wards; while among private patients the male sex predominates.

**Race.**—The Jewish race have, according to many, been disproportionately subject to diabetes. In the dispensaries of New York and Baltimore, this fact was very evident. The Hindus in India are peculiarly susceptible to this disease. It occurs not infrequently in the colored population. There are no available accurate data to determine whether or not the general impression that it is less common among them than among white people is warranted or not.

**Heredity.**—There can be no doubt that this malady is influenced by heredity in some cases. Von Noorden and Pleasants have each reported extensive family histories. A tendency has been noted by some authors for the onset of the diabetes to manifest itself at an earlier period in each successive generation. It commonly occurs in brothers and sisters.

It is interesting to note that Joslin claims that his cases of hereditary diabetes have frequently been mild and that this has so commonly been the case that he always looks upon heredity as a favorable omen.

*Diet.*—It has been very tempting to formulate theories concerning the effects of dietary excesses. Diabetes has been variously ascribed to the overindulgence in carbohydrates, especially sugar, or to the more luxurious diet, high in meat proteins, of the well-to-do. When all the facts are taken into consideration, it must be admitted that the proof of either contention is lacking.

*Obesity.*—Much emphasis has at times been put upon this feature as an etiological factor. That stout individuals, or those who once have been obese, suffer with diabetes mellitus, undoubtedly is true. In some of these, particularly in older persons, the disease is often very mild; on the other hand, especially in younger patients, some very severe types of the malady may develop. No relation except an empirical one has been formulated as existing between obesity and diabetes mellitus. There are many extreme examples of increase in weight, such, for instance, as are associated with hypopituitarism, in which diabetes does not occur. Furthermore, in hospital and dispensary cases, excepting the Hebrews, a history of obesity is the exception.

*Nervous Strain.*—How emotional stress may be responsible for a temporary glycosuria has already been discussed. The importance which has been laid upon nervous strain and shock in the causation of diabetes mellitus is probably in large part due to the fact that under these conditions an individual whose ability to utilize carbohydrates is below normal suffers still further impairment of this function, and as a result, true diabetes, which has hitherto been latent, may manifest itself. Trauma about the head and elsewhere is to be considered as producing glycosuria and diabetes only as far as it brings about shock.

*Arteriosclerosis* has often been thought to be an etiological factor in diabetes. It is supposed to interfere with the functions of the pancreas by curtailing the blood supply to this organ. Much confusion exists in regard to this subject, as most diabetics are of an age when arteriosclerosis often manifests itself, and it is a matter of common occurrence to have arteriosclerosis develop as a complication of diabetes.

*Syphilis.*—Various reports of the relation of syphilis to diabetes have been made. The proof that syphilis is a cause of diabetes would be a successful therapeutic test. Thus far antiluetic treatment has not proved to be of any value except in the rarest cases.

*Pregnancy.*—Frank considers that pregnancy increases the permeability of the kidney to sugar and that renal glycosuria exists in the majority of cases. Diabetes may make its appearance during pregnancy or be very much aggravated by it. Joslin takes a less pessimistic view of the situation, and believes it cannot yet be accepted as proven that pregnancy aggravates a diabetes.

*Gout.*—This has been looked upon as one of the traditional causative factors for diabetes. In America, at least, it seems to play a very small rôle. Gout is such a comparatively infrequent disease in this country that we may not be able to formulate a correct judgment of its influence.

*Acute Infections.*—It is undoubtedly true that the carbohydrate tolerance is much diminished by even a slight infection, such as an ordinary "cold," and the effect of more serious bacterial invasions may be correspondingly greater. Whether they may be the actual cause which

brings about diabetes is an entirely different question. It is probably best to reserve judgment on this point as well as the bearing of mouth infections. The latter may often be the result and not necessarily the cause of diabetes.

*Affections of the Bile Ducts.*—A history of gall stones is often obtained in cases of diabetes. It is probable that an occlusion of the distal portion of the bile duct system, common to the liver and pancreas, may result in a short circuiting of the bile into the pancreatic tissue with a consequent lesion in the islands of Langerhans. Biliary duct infections may follow the same course. The history of jaundice preceding the diabetes in Case A—detailed on the next page under “Symptomatology”—suggests such an etiology.

*Disorders of the Pancreas.*—The disturbances of the other glands with internal secretions have been considered under the head of glycosurias. This is a somewhat arbitrary classification, but inasmuch as the over-activity of the hypophysis, adrenal and thyroid glands was responsible for a diminished tolerance of carbohydrates whose etiology is different, whose clinical course is dissimilar and whose treatment in many respects is absolutely unlike that of diabetes mellitus, it has seemed wise to make this distinction.

The classical experiments of von Mering and Minkowski were the first of numberless observations which established the fact that the pancreas, besides its external intestinal secretion, gives rise to an internal secretion which in some way is responsible for the proper utilization of glucose. It is certain that in animals a destruction of the pancreas can bring about a disease picture which resembles diabetes mellitus in the human species very closely. If the pancreas is transplanted, or if it is incompletely extirpated, leaving approximately one-tenth or more of the gland substance within the body, or if the ducts of the pancreas are tied, diabetes mellitus does not ensue. A further study along these lines points to the islands of Langerhans as the probable source of this internal secretion. It is largely due to the efforts of Opie and his co-workers that the frequency of the lesions in these structures has been realized.

Disease of the pancreas, in which there may be destruction of the pancreatic tissue—carcinoma, calculus, acute and chronic pancreatitis, etc.—is not necessarily followed by glycosuria. McCallum's observations on the effects of ligation of the pancreatic ducts showed that the islands of Langerhans were the last portion of the pancreatic tissue to degenerate under these circumstances. This would seem to indicate that they are more resistant to disease than the remaining tissue and that they may still be well preserved though definite degenerative changes in the gland are present. While the islands are intact, diabetes does not manifest itself. These facts necessarily indicate that the islands of Langerhans are independently involved by a morbid process in the majority of instances of diabetes. It is very rare to meet with a case in which there is any evidence of deficiency of the external secretion of the pancreas. Frequent, large, fatty, foul-smelling stools is a symptom generally conspicuous by its absence. When such instances do occur, they have been designated as “pancreatic diabetes.”

The above statements should be regarded as the conclusions toward which the evidence points at present. How the internal secretion of the pancreas performs its function as an enzyme which actually acts



upon the glucose, as a detoxicant for some substance which interferes with the utilization of sugar or as a link which unites the glucose to the agents which digest it, is as yet entirely unknown. The older experiments on these questions were mostly worthless, as the presence of bacteria modified the results very greatly. Recently, Admont Clark has perfused the freshly extirpated bacteria-free heart and pancreas of the dog in series, and found that the glucose was not changed to carbon dioxid and water, but that more complex polysaccharids were formed from the glucose. The wonderful results now achieved by the injection of Banting's pancreatic extract "Insulin" bring the efforts of many physiologists to a successful clinical application.

**VALUE OF CONSIDERING THE ETIOLOGICAL FACTORS.**—While it must be admitted that the actual cause or causes of diabetes are not yet within our grasp, it should be recognized that all the factors mentioned above, as well as under the heading of glycosuria, should be carefully considered. In treating these cases, very much better results will be obtained if due attention is paid to emotional or nervous strain, to hyperthyroidism, to obesity, etc., than if they are neglected. It is a relatively common experience that a slight effort in remedying what are apparently negligible details will achieve big results.

**Symptomatology.**—**ONSET.**—The first symptom usually is glycosuria. The patient is not aware of its presence, unless it is discovered by accident in the course of a life insurance examination or a routine urine test. We are not well informed as to how long sugar may persist in the urine before the characteristic subjective symptoms of the malady become manifest. The following case history may be of interest, as illustrating how slowly this condition may develop and what importance should in certain instances be attached to transient glycosurias.

A——, age 36 at time of death in 1910, American. Urine, on Dec. 4, 1900, during an attack of severe catarrhal jaundice, was free from sugar. On Jan. 3, 1901, while the jaundice persisted, 1.3 per cent., and on Jan. 4, 0.4 per cent. glucose were found in a 12-hour specimen of about 900 c.c. The glycosuria disappeared at once on prohibition of sugar and moderate restriction of starches, and did not even recur after the resumption of a liberal mixed diet containing abundant sugar. Dec. 28, 1904, he developed left pyelonephritis, possibly from a small prostatic abscess. There was no sugar in the urine on Dec. 28 and 31 and Jan. 1. On Jan. 3, 1905, glycosuria appeared and persisted for a week; this was controlled by moderate dietary restrictions. In July, 1906, he was able to eat freely of toast, oatmeal, potato, rice and oranges without producing glycosuria; but any sugar or a single slice of untoasted bread would cause it. In July, 1907, a restriction of the starchy food did not render the urine sugar-free unless the proteins were limited as well; in Jan. 1908, this could only be accomplished by starvation. He died in diabetic coma in May, 1910.

For the first six years after the glycosuria had appeared, the progress of the disease was extremely slow; subsequently, it was very rapid.

In taking a routine history 2 or 3 years before death, the false impression of a stormy onset and a rapid course would have been obtained. This history may also be regarded of value in pointing out the stress which should be laid upon transient glycosurias as a possible indication of a lowered carbohydrate tolerance.

The first complaint of these patients is often pruritus, especially pruritus vulvæ. Weakness, loss of weight, thirst, increased appetite and polyuria form a syndrome which is very common. Furunculosis, an obstinate eczema, neuralgic pains, or in fact any of the symptoms or complications of the disease, may be the complaint which first brings the patient to his physician.

**FINDINGS IN THE URINE.**—The urinary signs which are looked upon as characteristic are a light color, a high specific gravity, an acid reaction, a positive test for acetone, diacetic acid and glucose, and an increased daily volume. It must be borne in mind that any or all of these may be lacking and still the specimen be that of a diabetic. The reprehensible habit of not testing for glucose because the urine is of low specific gravity, or lacks some other attribute, often leads to most embarrassing situations.

The *specific gravity* is generally about 1030 or higher. At times it is much lower in spite of the fact that an appreciable amount of glucose is present. The following are instances of this sort; in some patients, there are only isolated specimens in which the specific gravity is low, while the urine contains sugar; in others, this phenomenon is constant.

*24-Hour Specimens of Urine from Various Patients*

Specific Gravity	Glucose (Per cent.)	Specific Gravity	Glucose (Per cent.)
1024	3.4	1014	1.0
1022	2.0	1013	1.0
1019	1.4	1012	0.7
1018	1.3	1011	0.4
1017	0.4	1010	0.3
1015	1.7	1009	0.5

A low constant specific gravity may indicate that a nephritis with a considerable impairment of renal function exists and these cases should be investigated from this point of view. In some diabetics a polyuria and a low specific gravity persist almost indefinitely after the urine has been rendered sugar-free, although no nephritis or lesion of the urinary tract is present. It is probable that the hyperglycemia, glycosuria and polyuria in the preceding period during which these patients were not treated damaged the renal parenchyma in some way, so as to cause it to act in this manner. In these cases, no harm results from this urinary anomaly and it is inadvisable to treat it by water restriction or other measures.

The typical *amount of urine voided* in 24 hours by the diabetic is high. In the cases with considerable glycosuria it is usually in the neighborhood of 6 or 7 liters, although in many instances very much larger quantities have been recorded. It is not infrequent, however, to find instances in which the urinary volume is not only not increased, but has a tendency to be subnormal. It is important to realize that a patient may void a normal quantity of urine and yet be suffering with diabetes and glycosuria. Such cases have been designated as diabetes decipiens. Consecutive 24-hour specimens from such patients are as follows:

Case 1.	Urine Volume 24 hrs. c.c.	Glucose (Per cent.)	Case 2.	Urine Volume 24 hrs. c.c.	Glucose (Per cent.)
	780	1.1		840	2.5
	600	1.3		920	1.4
	1400	0.6		710	0.6
	730	1.1	Case 3.		
	770	1.6		970	3.3
	690	1.4			

As the quantity of sugar increases, the volume of urine rises, but not as rapidly, so that the percentage of glucose is generally greater in larger 24-hour specimens. This may be gathered from the following table, taken from Von Noorden:

<i>Relation of Volume of Urine to the Percentage of Glucose</i>	
Urine Volume 24 hrs. c.c.	Glucose (Per cent.)
1,500- 2,500	2-3
2,500- 4,000	3-5
4,000- 6,000	4-7
6,000-10,000	6-9

*Nocturia.*—It is only to be expected that when the volume of the urine rises it should be accompanied by increased frequency of voiding at night. This is important, since bed wetting in children who have previously been free of the habit is often the first sign of the presence of diabetes.

*Glycosuria.*—The laboratory tests for glycosuria have already been described under "The Identification of Glucose in the Urine." In examining the urine for sugar, it is desirable to examine 24-hour specimens and to be careful to avoid the first specimen voided in the morning, as this, representing, as it usually does, the fasting period of the last half of the night, is frequently free from sugar, whereas the urine of the afternoon or evening may yield a positive reaction. Besides establishing the presence or absence of glucose in the urine and its cause according to the methods already detailed, it is necessary to estimate the percentage of sugar and the total quantity excreted in the 24 hours. Many methods have been advocated for this estimation, but it is only within a comparatively recent time that satisfactory ones have been devised. The original *Fehling's solution* yields an end point which is exceedingly difficult to read. The use of the polariscope is simple, but requires two readings, the first on the urine as voided, the second after the glucose has been removed by fermentation. It is only in this way that allowance can be made for the levorotatory substances that occur in any urine, and especially for the beta-oxybutyric acid so often present in considerable quantities in the diabetic. These steps materially delay the results and constitute a considerable drawback. The method devised by Benedict has found universal acceptance and is probably the most valuable clinical means we have for quantitating the sugar in the urine.

*Benedict's Modification of Fehling's Solution for the Quantitative Estimation of Sugar in the Urine.*†—The solution which will keep indefinitely is as follows:

	Grams or c.c.
Copper sulphate (pure crystallized).....	18.0
Sodium carbonate (crystallized)*.....	200.0
Sodium or potassium citrate.....	200.0
Potassium sulphocyanate.....	125.0
Five per cent. potassium ferrocyanid solution.....	5.0
Distilled water to make a total volume of.....	1,000.0

\* One-half the weight of the anhydrous salt may be used.

With the aid of heat dissolve the carbonate, citrate and sulphocyanate in enough water to make about 800 c.c. of the mixture, and filter if necessary. Dissolve the copper sulphate separately in about 100 c.c. of

† Benedict, S. R., *Jour. Am. Med. Ass'n*, 1911, lvii, 1193.

water and pour the solution slowly into the other liquid with constant stirring. Add the ferrocyanid solution, cool and dilute to exactly one liter. Of the various constituents, the copper salt only need be weighed with exactness. Twenty-five c.c. of the reagent are reduced by 50 mg. of glucose.

Sugar estimations are conducted as follows: The urine, 10 c.c. of which should be diluted with water to 100 c.c. (unless the sugar content is believed to be low), is poured into a 50 c.c. buret up to the zero mark. Twenty-five c.c. of the reagent are measured with a pipet into a porcelain evaporation dish (25-30 cm. in diameter), 10 to 20 grams of crystallized sodium carbonate (or one-half the weight of the anhydrous salt) are added, together with a small quantity of powdered pumice-stone or talcum, and the mixture heated to boiling over a free flame until the carbonate has entirely dissolved. The dilute urine is now run in from the buret, rather rapidly, until a chalk-white precipitate forms, and the blue color of the mixture begins to lessen perceptibly, after which the solution from the buret must be run in a few drops at a time, until the disappearance of the last trace of blue color, which marks the end-point. The solution must be kept boiling vigorously throughout the entire titration. If the mixture becomes too concentrated during the process, water may be added from time to time to replace the volume lost by evaporation. The calculation of the percentage of sugar in the original sample of urine is very simple. The 25 c.c. of copper solution are reduced by exactly 50 mg. of glucose. Therefore the volume run out of the buret to effect the reduction contained 50 mg. of the sugar. When the urine is diluted 1:10, as in the usual titration of diabetic urines, the formula for calculating the per cent. of sugar is the following: 
$$\frac{0.050}{X} \times 1,000 = \text{per cent. in original sample, wherein } X$$
 is the number of cubic centimeters of the diluted urine required to reduce 25 c.c. of the copper solution.

In our laboratories very satisfactory results could be obtained with hand pipets and undiluted urine. This makes the procedure somewhat simpler.

Joslin advocates the use of only 5 c.c. of the Benedict-Fehling solution for the test. This effects a great economy in a rather expensive reagent.

**RESULTS OF POLYURIA.**—Whenever polyuria is present, there is a proportional degree of *thirst*. In many cases the urine volume is so large that the intake of fluid no longer balances the output and a certain degree of *desiccation* results. The dry skin, the high color of the face about the cheek bones, giving the impression of an existing fever, the marked constipation, and in part, at least, the lassitude and malaise, may all be attributed to lack of available water in the tissues.

The **APPETITE** is *increased* when there is a glycosuria of any consequence. The ravenous desire for food which the improperly treated cases exhibit makes a most distressing vicious cycle. The more they eat, the greater is the output of glucose and the caloric loss in the urine and the more urgent the polyphagia becomes. When the urine is rendered sugar-free, this symptom promptly disappears.

**LOSS OF WEIGHT AND EMACIATION.**—It is a natural sequence of the increasing excretion in the urine of materials which represent many available calories to the normal organism, that loss of body weight, which

may often be extreme, and weakness should ensue. Such a deplorable state of affairs can usually be checked and often much improved by suitable treatment. It has already been shown how all of the carbohydrates may appear quantitatively in the urine as glucose and how 58 per cent. of protein food may meet the same fate. Besides glucose, the so-called acid substances, beta-oxybutyric acid, diacetic acid and acetone may be excreted by the kidneys. Their significance and mode of formation has

TABLE 7  
LOSS OF CALORIES IN "COMPLETE" DIABETES

	In 100 Grams of:		
	Carbohydrate	Fat	Protein
Calories lost as glucose.....	410	0	238
Calories lost as B-oxybutyric acid.....	0	162	162
Total calories lost.....	410	162	400
Calories utilized.....	0	768	10
Calories available in a normal man.....	410	930	410

been more thoroughly discussed under Acidosis. In the present section, it is desired only to call attention to the fact that 36 per cent. of protein and 36 per cent. of fat may be eliminated in the urine as one or other of the acid substances, and that the caloric value of one gram of beta-oxybutyric acid is 4.5 calories. Summarizing the above statements in Table 7, it is seen that the "complete" diabetic, who can no longer utilize any carbohydrate, and is excreting the maximal amounts of acid substances, is deriving nourishment from such a small portion of his food that death from inanition is an inevitable result, unless relief is obtained by the administration of insulin. The table represents the ultimate state of metabolism of the diabetic; the intermediate stages, of course, are less threatening but yet of considerable importance from the nutritional point of view.

ACIDOSIS and its symptoms have already been discussed.

**CARBOHYDRATE TOLERANCE.**—Tests for carbohydrate tolerance and their significance have been fully taken up elsewhere, and need only be referred to here.

**History Forms.**—The proper recording of symptoms, etiological factors, etc., in taking the history in a case of diabetes is virtually impossible unless there is some set form to act as guide. The use of such an outline makes future reference in a chronic disease such as diabetes very easy. The author has found the following scheme of very material assistance. It requires some time to fill out this blank the first time the patient is seen, but much labor and effort are done away with subsequently. The accompanying form (plates I, II, III) has been used at the New York Post Graduate Hospital and several other clinics and for private patients, with a good deal of satisfaction.

**Complications.**—Diabetes is remarkable for the number of complications that may occur in the course of the malady. Some of these are found so frequently that they could almost be classed in the category of symptoms. The presence of any of the untoward manifestations usually regarded as complications should lead the medical adviser to suspect diabetes as the etiological factor.

**SKIN.**—The presence of boils and carbuncles in this condition is extremely common. The former can generally be controlled; the latter

**PLATE I**

<b>NAME</b>		<b>DISPENSARY No.</b>	
Address	Age	Date	
	Sex	S. M. W.	
Race	Birthplace	Occupation	
Religious Ancestry			
<b>METABOLISM CLINIC</b>		<b>DIABETES MELLITUS</b>	
DIAGNOSIS:			
History taken by			
<div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p><b>1 HEREDITY, DIABETES MELLITUS</b></p> <p>Goitre</p> <p>Gout</p> <p>Obesity</p> <p>Tuberculosis</p> <p>F.</p> <p>Brothers</p> </div> <div style="width: 45%;"> <p>Heart Disease</p> <p>Nephritis</p> <p>Apoplexy</p> <p>M.</p> <p>Sisters</p> </div> </div>			
<div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p><b>2 PERSONAL, ALCOHOL</b></p> <p>Tobacco</p> <p>Genital</p> </div> <div style="width: 45%;"> <p>Tea</p> <p>Coffee</p> <p>Dietary Habits</p> </div> </div>			
<b>3. PAST HISTORY</b>			
<b>4. SUGAR FIRST DISCOVERED</b>			
<b>5. ONSET, DATE, SYMPTOMS</b>			
<b>6. POSSIBLE PRECEDING SYMPTOMS</b>			
<b>7. WHY WAS URINE EXAMINED FOR SUGAR?</b>			



## PLATE II

### 8. POSSIBLE ETIOLOGY (Describe and give duration and date of each symptom)

- |   |  |
|---|--|
| <p><i>a.</i> Obesity</p> <p><i>b.</i> Traumatic</p> <p><i>c.</i> Nervous</p> <p><i>d.</i> Pancreas, Abdominal Pain</p> <p style="padding-left: 20px;">Character of Stools</p> <p><i>e.</i> Thyroid, Exophthalmos</p> <p style="padding-left: 20px;">Thyroid Enlargement</p> <p style="padding-left: 20px;">Vomiting</p> <p style="padding-left: 20px;">Nervousness</p> <p style="padding-left: 20px;">Tremor</p> <p style="padding-left: 20px;">Cardiac Palpitation</p> <p style="padding-left: 20px;">Diarrhea</p> | <p><i>f.</i> Hypophysis, Acromegaly</p> <p style="padding-left: 20px;">Gigantism</p> <p><i>g.</i> Kidney, Headache</p> <p style="padding-left: 20px;">Visual Disturbances</p> <p style="padding-left: 20px;">Dyspnea</p> <p style="padding-left: 20px;">Vertigo</p> <p style="padding-left: 20px;">Edema</p> <p style="padding-left: 20px;">Albuminuria</p> <p><i>h.</i> Liver, Skin Pigmentation</p> <p><i>i.</i> Unknown</p> |
|---|--|

### 9. PREVIOUS TREATMENT AND RESULTS

### 10. SYMPTOMS SINCE ONSET OF DISEASE (Date of each and relation to any treatment)

- |   |  |
|---|--|
| <p><i>a.</i> Weight,.....Lbs. to-day</p> <p style="padding-left: 40px;">.....Lbs. Highest.....19</p> <p style="padding-left: 40px;">.....Lbs. at Onset</p> <p style="padding-left: 40px;">.....Lbs. Loss From Highest W't</p> <p><i>b.</i> Loss of Strength</p> <p><i>c.</i> Polyuria</p> <p><i>d.</i> Nocturia</p> <p><i>e.</i> Polydipsia</p> <p><i>f.</i> Polyphagia</p> | <p><i>g.</i> Skin; Pruritus</p> <p style="padding-left: 20px;">Furunculosis</p> <p style="padding-left: 20px;">Other conditions</p> <p><i>h.</i> Pains</p> <p><i>i.</i> Extremities</p> <p><i>j.</i> Cramps</p> <p><i>k.</i> Mouth</p> <p><i>l.</i> Bowels</p> |
|---|--|

### 11. OTHER SYMPTOMS

- a.* Digestive
- b.* Circulatory
- c.* Renal
- d.* Respiratory
- e.* Nervous
- f.*

### 12. PRESENT COMPLAINT





are of serious portent, many of these cases terminating fatally. Pruritus of the entire skin or only of the genitals is often found. The fermentation and irritation set up by the glucose in the urine is responsible for the local itching, and generally this disappears promptly when the glycosuria is controlled. The general pruritus occurs comparatively rarely. It is difficult to determine the cause for it. The hyperglycemia alone cannot be made responsible, as the itching is not present in the majority of cases when there is an excess of sugar in the blood, nor does it always disappear when the glucose is eliminated from the urine and reduced in the blood. Xanthoma is a rare and interesting finding. A purpura, when present, is usually to be associated with cachexia. *Gangrene* of the extremities, especially the legs, and *perforating ulcer*, the *mal perforans* of diabetes, are not uncommon. These complications may be assigned to a triple etiology: (1) *Trophic*: In many of these cases the knee-jerks are absent, and the changes often are very similar to those occurring in true tabes. (2) *Arteriosclerosis*: The dorsalis pedis vessel often is obliterated and no pulsation can be elicited in it. (3) *Hyperglycemia*: Exactly what bearing the excess of glucose in the blood has is hard to determine, but that it has some influence is attested to by the marked improvement in many of these cases when they are treated by diet. There is a considerable danger of infection in these instances. Such patients should be treated conservatively, unless there is a progressive cellulitis in the neighboring tissues, when thorough drainage is often the only remedy that will avert serious consequences. In rare cases a condition known as hemachromatosis, bronzed diabetes, or *diabète bronzé* occurs. This disease presents the combined symptoms associated with cirrhosis of the pancreas and liver, as well as the discoloration of the skin caused by two pigments, hemosiderin, which is brown in color and contains iron, and hemofuscin, which is ochre-yellow and iron-free.

**HEART AND BLOOD-VESSELS.**—Hypertension, as Janeway says, is peculiarly common in elderly diabetics. Diabetes in itself will not, as a rule, cause an increased blood-pressure. It is only after the disease has persisted for some years that this may become manifest. What rôle the diabetes plays and how far advancing years may be responsible for this change, it is hard to say. Janeway's statistics indicate that after 40 the diabetic gives evidence of a distinctly augmented blood-pressure, as compared to the normal person. The writer's impressions would lead him to the same conclusion. It has been previously mentioned that arteriosclerosis and its sequelæ (cerebral hemorrhage, etc.) are prone to terminate the life of the diabetic who escapes the more serious effects of his metabolic disturbances. Arteriosclerosis, in any event, often develops at an earlier period than usual, and by affecting vital vessels in the brain, heart or kidneys, may result in marked changes in those organs. It may be that hypertension has an influence on the arteries in this connection. Cardiac insufficiency because of a weak heart muscle, brought on in part by inadequate nutrition and in part by changes in the coronary vessels, caused by the agencies mentioned above, may in some long-standing cases make itself felt.

**KIDNEY.**—*Albuminuria* may be noted frequently. A severe nephritis with hypertension is not uncommon. A few of these cases studied by the writer would seem to indicate that the hypertension develops first and that the renal changes come later; in other words, that there is

often a *primary contracted kidney*. Some authors have held that such cases exhibited a higher renal threshold to sugar and that their condition actually improved. When diabetes and marked interstitial nephritis coexist, it is a difficult question on theoretical grounds whether the high protein diet necessary for the former or the high carbohydrate feeding suitable for the latter should be ordered. The writer, from his experience, believes this to be a theoretical question only; from the practical point of view these cases have always been most benefited when they have been treated as though they had diabetes only and no nephritis.

*Edema* is of very frequent occurrence and often assumes almost alarming proportions. There may be hydrothorax and ascites as well as fluid in the subcutaneous tissues. If there is no marked cardiac weakness or renal insufficiency, this symptom usually clears up and no apprehension need be felt concerning it. The green day and oatmeal diets, used until replaced by other methods of feeding, were frequently accompanied by marked edema. During the past years it has gradually been realized that the retention of fluid in diabetes may be brought about by administration of bicarbonate of soda (Table 8) or sodium chlorid, and that when these substances are withheld the edema disappears. This enables the physician in many instances to control a very essential factor in metabolism. Allusion has already been made to the weakness, malaise and marked constipation that accompany desiccation. These symptoms can be cleared up in a very short period when moderate fluid retention is brought about by the use of sodium bicarbonate or chlorid. By some authors the beneficial action of edema has been noted in the empirical observation that cases exhibiting edema do not go into diabetic coma. This is true in most instances, though the writer has seen one case of diabetic coma in an edematous patient. Diuretics, especially theocin, have been advocated to stimulate the flow of urine. It is rarely necessary to use them; the control of the two salts mentioned above usually suffices. An example of what proportions edema may assume may be gathered from the data of the following case:

TABLE 8

DATA OF A CASE OF DIABETES MELLITUS INDICATING THE PARALLELISM BETWEEN EDEMA FORMATION (AS SHOWN BY THE FLUID BALANCE AND FLUCTUATION IN WEIGHT) AND THE ADMINISTRATION OF BICARBONATE OF SODA

Date	Fluid (c.c.)			Weight (Lbs.)	Bicarbonate of Soda (Grams)	Remarks
	Intake	Urine	Balance			
Nov. 1....	2240	1200	+1040	84	30	Considerable edema.
2....	2880	1320	+1560	84½	30	
3....	2700	1110	+1590	89	30	
4....	2580	1560	+1020	91	30	
5....	2370	1140	+1230	91½	30	
6....	2220	1470	+ 750	93	0	Extreme edema.
7....	2340	2340	0	92½	0	
8....	2220	1650	+ 570	91½	10	
9....	1920	2370	- 450	90	0	Edema diminishing.
10....	2040	2730	- 690	87	0	
14....	2400	2790	- 390	76	0	
17....	1920	1680	+ 240	74	10	No edema.
21....	2580	1290	+1290	72	10	
23....	3240	1920	+1320	72½	15	

**LUNGS.**—Pulmonary tuberculosis was formerly dreaded as a frequent complication in diabetes. Montgomery came to the conclusion that tuberculosis is not more common in this disease than it is in the population at large. This is the experience of most physicians who

come in contact extensively with either malady. If a patient is afflicted with both diabetes and tuberculosis, the best results—and they are often most satisfactory—are obtained when the dietetic treatment is directed primarily against the diabetes.

*Pneumonia* followed by *gangrene* is said to be a common event. In the experience of many of us, both the pneumonia and its sequel are rare.

**DIGESTIVE SYSTEM.**—*Pyorrhœa alveolaris* and its sequelæ are evidently favored by the diabetes. Digestive upsets, nausea, vomiting and diarrhea may precede the onset of coma. At other times they may develop if a patient indulges excessively in carbohydrates, exceeds his tolerance and becomes prey to an insatiable desire for food. The diarrhea in these cases may be an extremely obstinate one. An occlusion of the pancreatic duct or destruction of the whole pancreatic gland will give rise to characteristic stools, which are very voluminous, contain neutral fat and undigested meat fibers, have a foul odor and give negative reactions for the pancreatic ferments.

**NERVOUS SYSTEM.**—The coma characteristic of diabetes has been described under *Acidosis*. The knee-jerks are entirely lacking or much diminished in many cases. Where the lesion lies that is responsible for this change has not been definitely determined. It may be in the posterior columns of the cord or in the peripheral nerves. There have not been sufficient anatomical investigations to determine this point. The possible trophic relations of this involvement of the nervous system to perforating ulcer of the foot have been pointed out. Pain may be very marked. The other symptoms of *tabes*, such as the lack of reaction of the pupils to light, the bladder and rectal disturbances, etc., are absent. This condition has been termed the *pseudo-tabes of diabetes*. Pains which occur most frequently in the lower extremities but may be brought about by a *neuritis* in any other part of the body are extremely troublesome as well as frequent. *Paresthesiæ* and *muscular cramps* especially in the calves of the legs are often present. The latter may be associated with the desiccation characteristic of this disease; they are prone to occur in the early morning hours; they are sometimes the initial symptom of which the diabetic complains. The neuritis is in many instances completely relieved when a proper dietary regimen is instituted and the urine rendered sugar-free. However, care must be taken not to promise relief to these patients, as all therapeutic effort may at times be ineffectual.

**SPECIAL SENSES.**—*Cataract* is prone to develop. *Retinitis* is of frequent occurrence. This has been designated as diabetic retinitis. All examples of this complication which the author has seen have occurred in diabetics in whom there was associated nephritis, arteriosclerosis or hypertension and the retinal changes have appeared to have the characteristics usually manifested by the eye-grounds in these conditions. Optic nerve atrophy, paralysis of the extrinsic eye muscles and amaurosis occur occasionally. Otitis media, impaired hearing and deafness may develop.

**Clinical Types.**—Various attempts have been made to classify diabetes mellitus into mild, moderately severe, and severe types, according to the response to diet. The criterion according to which the cases were graded was their tolerance for carbohydrates. The advances during the past few years have nullified nearly all these attempts of systematizing our ideas. If it was true a few years ago that the response of diabetes

mellitus to diet frequently improved a patient's condition to such a degree that he passed from one type to another in a rather disconcerting manner, it becomes an impossibly intricate maze of reasoning to follow the sugar burning capacity of such cases accurately when insulin is employed. The whole scheme of such classifications had best be discarded and in describing cases of diabetes they may be roughly pigeon-holed as having a tolerance for a certain diet estimated in grams of protein, fat and carbohydrate while receiving none or a given number of units of insulin.

From another point of view diabetes mellitus may be classified as either acute or chronic. There may be acute exacerbations of chronic states. It is very valuable in the subsequent guidance of a patient to be accurately informed concerning the previous events in this regard, as history is prone to repeat itself; a diabetic whose condition has been either stationary or progressive is prone to continue in the same manner in the future. If nervous strain, an infection, an attack of biliary colic or other episodes have resulted in a serious aggravation of the diabetic symptoms in the past they are likely to do so again.

Two extremes may be cited to show how wide a variation in the type of diabetes may occur:

A member of the Officers' Training Corps was brought into a base hospital and in less than two days died of diabetic coma; investigation disclosed that he had passed several physical examinations, including urinary analyses, a short time previously and nothing abnormal had been discovered; his room-mate noted that two weeks before his death sudden intense thirst and polyuria had set in; this may be considered to be a case of acute fatal diabetes mellitus of only a few days' duration. This history is in marked contrast with that of a man forty-eight years old who was rejected on life insurance examination ten years previously because of the presence of albumin and sugar in the urine. The medical examiner met him a year later and is reported to have involuntarily exclaimed: "Man, are you still alive?" This spurred the diabetic to action and on the advice of a friend he treated his albuminuria by a low protein diet which he has continued since that time. The diet is worth considering:

Breakfast: 2 glasses of milk.

Lunch: 2 eggs, 4 to 6 rolls, butter.

Dinner: Clear soup, meat about 8 ounces, vegetables, potatoes,  $\frac{1}{2}$  loaf of bread, butter and fruit.

10 P.M.: Glass of milk.

For four years much beer was indulged in; for the last six years none was taken.

It is scarcely credible that this man should live ten years after breaking every rule that was ever formulated for the care of diabetes. However, he had lost no weight, in fact, was obese, weighing 225 $\frac{1}{2}$  pounds, the height being 5 feet 8 $\frac{1}{2}$  inches; there were no signs or symptoms giving any evidence of thyroid or pituitary disturbance; there were only two signs or symptoms, besides a very marked glycosuria, that could be referred to the diabetes, these were impotence and absent knee-jerks.

Thus far no noteworthy attempt has been made to differentiate the benign or stationary and the malignant or progressive type of diabetes. In a general way it is known that children exhibit the severest form of the disease but even here exceptions occur. Why does one case progress rapidly while the other does not? The answer of this question is probably to be found in the cause of diabetes. It is realized that changes in the islands of Langerhans in the pancreas bring about a diminished ability to utilize starches; but what factors, in turn, are responsible for such pathologic lesions? Infections even of slight degree may often cause an exacerbation of an existing diabetes; therefore, it may be assumed that the absorption of toxic material from an infective focus

may be to blame in some cases; the blocking of the common bile-duct and forcing of bile into the pancreas is another recognized cause; pancreatic calculi may be responsible in some cases; arteriosclerosis of the pancreatic vessels undoubtedly results in some of the slowly advancing types in elderly individuals, in the main, however, there is little known concerning the cause of the pancreatic lesions. If this knowledge were at hand some cases might be cured.

If there are multiple causes for the changes in the islands of Langerhans some of which are presumably active for only a short period, while others are constantly bringing about further pancreatic damage, then there must be some instances in which there is acute disease which subsequently does not progress, whereas others must exist in which the constant deterioration of the pancreatic tissue is distinctly evident.

It would be a very great advantage if these clinical types could be distinguished one from the other. At present the attempt is made to treat them all alike. No one treats all cases of pulmonary tuberculosis, whether they are active or inactive, in precisely the same way. However, that is to a great extent the scheme of dietetic therapy that is being accorded the individual that is suffering with diabetes mellitus. The past history of any case furnishes a distinct clue as to how rapidly the condition has advanced; the disease, as is well known, is more prone to be severe in the young than in the old; nervous alert individuals are more subject to exacerbation than those with a placid disposition, obese diabetics are often found to progress very slowly; there are many exceptions to the above statements but they and many other facts that will have to be developed will serve to point out the way for the most suitable dietetic therapy.

The terms mild and severe as used in these pages refer to a good or a poor carbohydrate tolerance.

**Treatment.**—In the treatment of this disease, we are very fortunate in being able to control our results with great accuracy by means of laboratory tests. It is now well established that, if the urine is sugar-free, there is no undue strain put upon the functions which utilize the carbohydrates, and that under these conditions the best chances are offered for progress toward recovery. In some instances there is very marked improvement; in others, the disease is only checked; while in still others it must be admitted a slow but certain downward progress takes place in spite of our best efforts. However, in no case should therapy be neglected. It is only those who have witnessed the pitiful fate of the sufferers with this disease who have thrown all dietary precautions to the winds that realize what torture they may be subjected to. The emaciation, incessant voiding, extreme weakness, furunculosis, perforating ulcers, which often become infected, cataract and other complications, make such patients impressive object lessons. Many diabetics boast of how they can maintain sugar in the urine, eat what they desire, and nullify most of the medical ideas concerning their condition. It is perfectly true that there are some instances in which such a rash scheme may be carried out with impunity. Such individuals create a certain degree of skepticism among their fellow sufferers, and sometimes obtain a hearing with the medical profession. However, these patients are prone to be very silent when the results of their carelessness overtake them, and then it is usually too late to atone for past transgressions. It should be most forcibly impressed upon any one who has

diabetics entrusted to his care that the only safe procedure is to keep the urine free from sugar. A case, however mild it may appear, whether in the old or in the young, may progress rapidly and every prophylactic measure should be taken to forestall this possibility.

It is now generally admitted that **dietetic therapy** and the use of **insulin** are the only means by which we can combat this disease. Drugs, such as *urotropin*, *atropin*, *arsenic*, *morphin*, excepting insulin, the various *preparations derived from the endocrine glands*, etc., have all received their full share of attention and been found wanting. The so-called cures at the German spas and elsewhere invariably depend upon regulation of the diet, however subsidiary this may be made in order to tempt the patient who is not satisfied with routine treatment at home.

The keystone upon which the therapy rests is to render the urine sugar-free. This results in a more efficient utilization of the carbohydrates, which in turn sets aside or diminishes the acidosis and causes a lowering of the blood-sugar level. The success of therapy in these regards demands a great deal of adjustment to the needs of the individual patient and it is easiest to achieve if the three objects of treatment are kept in mind separately: The control of (1) Glycosuria; (2) Acidosis; (3) Blood Sugar.

1. **DIETETIC THERAPY.**—(a) *Mild or Early Cases.*—In some patients it is only necessary to limit the carbohydrates and restrict none of the other articles of food. Such cases can be easily and effectively handled in the office or dispensary. A convenient diet list under these circumstances is that designated as **starch-free diet**, qualitative list. These dietary directions are simple and are arranged so that they are easily understood and carried out.

#### STARCH-FREE DIET

##### *Qualitative List*

##### *May Eat:*

- Soups—Clear meat broths, which may contain the vegetables indicated below.
- Meats—All kinds of meat, fresh, smoked or cured, except liver; all meats must be prepared without flour or bread-crumbs.
- Fish—All kinds of fish, but no clams, oysters or scallops.
- Eggs—Eggs in any form, prepared without milk, flour or sweetening (sugar, jam, etc.).
- Butter—Butter, oil and lard.
- Cheese—All kinds of cheese.
- Vegetables—Asparagus, asparagus tips, brussels sprouts, cabbage, cauliflower, celery, cucumbers, egg plant, endive, greens from beets, kohlrabi, leeks, lettuce, pickles (sour or dill), pumpkin, radishes, rhubarb, sauerkraut, sorrel, spinach, string beans, swiss chard, tomatoes, water cress, wax beans.
- Desserts—Gelatine jellies (use sour white wine, brandy or coffee for flavoring).
- Beverages—Tea, coffee and cocoa made from cracked cocoa (cocoa nibs), sweetened with saccharine (without sugar or milk); claret, burgundy, sour white wine, and whiskey in moderate amounts; carbonated waters.
- Condiments—Pepper, salt, mustard, oil, vinegar, saccharine.

##### *Must Avoid Eating:*

Sugar in any form. Bread, biscuits, and cakes of all kinds. Toast, crackers, rice, oatmeal (and all cereals); sago, tapioca, macaroni, vermicelli, potatoes, carrots, parsnips, beets, corn, beans, peas. All fruits fresh, preserved and dried. Jams and jellies. Pastry, puddings and ice cream. Sauces and gravies thickened with flour.

*Must Avoid Drinking:*

Milks, ales, porter, stout, beer, cider, all sweet wines, port wine, liqueurs, sparkling wines, syrups.

An example of a patient treated by this method is the following:

TABLE 9  
URINE AND DIET CHART

C. D. C. AGE 38. DIABETES MELLITUS

Date	Vol. 24 Hrs. (c.c.)	Glucose		Carbohydrate		Ace- tone	Diace- tic Acid	Weight (Lbs.)	Diet
		Per cent.	Gms.	In- take	Balance				
1913									
May 8..	4500	7.0	315.0	?	?	0	0	136	Lax, as customary.
13..	1920	3.0	57.6	90	+32	++	Trace	136	C. F.,* 11 Uneeda biscuit,
									½ grape-fruit.
20..	1440	3.1	44.6	65	+20	++	++	139	" 6 Uneeda biscuit,
									½ grape-fruit.
June 3..	960	0.2	1.9	35	+33	++	++	144	" ½ grape-fruit.
17..	1800	0.0	0	35	+35	+	+	147	" ½ "
23..	1440	0.0	0	50	+50	+	+	143	" 1 "
July 8..	1400	0.0	0	70	+70	+	Trace	144	" 3 Uneeda biscuit,
									1 grape-fruit.
22..	1440	0.0	0	85	+85	+	0	144	" 6 Uneeda biscuit,
									1 grape-fruit.
Aug. 5..	2400	0.0	0	100	+100	+	0	146	" 9 Uneeda biscuit,
									1 grape-fruit.
19..	1500	0.1	1.5	85	+33	0	0	145	" 9 Uneeda biscuit,
									2½ peaches.

\* C. F. is an abbreviation for carbohydrate- (or starch-) free diet.

*Ambulant Treatment of a Case of Diabetes Mellitus.*—Note: the disappearance of polyuria and glycosuria; the increase of weight which was accompanied by an increase in strength and enabled the patient to resume his active work; the absence of any severe grade of acidosis; a carbohydrate tolerance of about 100 grams. The subsequent diet of this patient should have contained 70 grams of carbohydrate every day of the week except one, when a carbohydrate-free diet should have been taken.

When these patients are first seen, they very frequently have had no treatment, and are apt to exhibit extreme degrees of polyuria and glycosuria, associated with loss of weight and strength. The immediate course which is to be pursued by dietetic therapy must be largely shaped by the physician's judgment and by the willingness of the patient to enter a hospital or obtain suitable nursing at home. Granting that the patient's immediate welfare is not threatened by acidosis, emaciation or weakness, ambulant treatment may be advised. Under these circumstances, it is wise to be conservative at first. With an absolute restriction of starchy foods in the diet, it is not an uncommon event to have the symptoms of acidosis develop with extreme suddenness and severity. To avoid this possibility, a considerable amount of carbohydrate may be added to the starch-free diet. In the case under consideration (Table 9) this was contained in the 11 Uneeda biscuits and ½ grape-fruit. (Uneeda biscuits form a very convenient and fairly accurate way of measuring the carbohydrate content of the diet, when food scales are not available. Uneeda biscuits have no further advantage over other starchy foods.)

The so-called **carbohydrate-free diet** contains a moderate amount of starch, principally in the green vegetables. This may be roughly estimated as being equivalent to 15 grams. The amount of starch which should be allowed a new patient at the beginning of treatment will



naturally vary with the severity of the case. In the present instance, the high percentage and quantity of sugar in the urine made it advisable to order what was thought to be the equivalent of 90 grams (page 107).

It may be readily seen from Table 9 that even under these circumstances, moderate amounts of acetone and diacetic acid appeared in the urine. However, these were not present in alarming quantities, and the diet was gradually cut down in spite of their presence until the reaction for glucose was negative. Subsequently, the amount of starch was increased, until sugar again appeared in the urine. At this point, when about 100 grams of starch were given, the patient's carbohydrate tolerance had evidently been reached. In treating such cases further, a good rule is to allow them in their daily diet 30 per cent. less of starch than their upper limit of tolerance, and to give one day a week on which the quantity of starch is very much curtailed. In the present instance, therefore, the patient should be ordered a daily diet containing 70 grams of carbohydrate, and on one day of the week, a starch-free diet. In the course of the next two or three months, the carbohydrate tolerance should be determined again, because with the restrictions imposed, it would be possible that his ability to utilize glucose would be increased materially, and the starchy food might be proportionately added to.

Attention should be called to the fact that some clinicians advocate the use of starvation or insulin in every case of glycosuria, however mild it may be. This does not appear to be necessary unless carbohydrate tolerance cannot be built up by the means outlined above.

It is a very tedious but very necessary procedure to order the carbohydrate-containing foods with precision. In this connection, the following tables are suggested as useful:

ATWATER AND BRYANT: U. S. Dept. of Agriculture, Bull. No. 28, 1906.

LOCKE: "Food Values," New York, 1911.

STREET, JOHN PHILLIPS: Report of the Connecticut Agricultural Station on Diabetic Foods.

The first two of these are valuable in computing the caloric, protein, fat and carbohydrate values of all the foods; the last is applicable only to diabetic foods, and is of inestimable service in this connection. Questions are constantly asked by patients concerning the advisability of using any number of so-called diabetic foods, and unless the physician is prepared to answer these inquiries by resorting to a manual of this sort, much dissatisfaction is frequently engendered. A table which has given considerable satisfaction is the one designated as the **accessory diet of foods rich in carbohydrates** (page 107). All the starch-containing food substances are given in amounts both in grams and in household measures as the equivalent of the ordinary slice of bread which contains approximately 15 grams of starch. Intelligent patients with a considerable degree of carbohydrate tolerance can employ this table with safety, making their own substitutions and gratifying their desires in every possible way. With the less intelligent classes, more specific directions and more marked limitations must be adhered to. These the physician can readily designate by resorting to the table under consideration.

TABLE 10

## ACCESSORY DIET OF FOODS RICH IN CARBOHYDRATES \*

If the patient's urine continues to be sugar-free on a "carbohydrate-free" diet of sufficient caloric value, carbohydrate-containing foods may be added and the carbohydrate tolerance of the patient be determined. In those cases able to utilize a considerable amount of starch, the accessory diet may be varied from day to day, and use may be made of the following table, which gives the carbohydrate equivalent of one slice (1 ounce or 30 grams) of white bread, containing approximately 15 grams of starch.

Foods	Household Measure	Gm.	Foods	Household Measure	Gm. c.c.
<i>Uncooked Flours, etc.</i>			<i>Fruits</i>		
Barley.....	1 H. Tbsp.	21	Apple.....	1 Medium	120
Buckwheat.....	1 "	19	Apricots.....	2 Large	120
Cornmeal.....	1 "	20	Banana (without skin).....	1/2 Medium	75
Farina.....	1 "	20	Cherries.....		90
Hominy.....	1 "	18	Currants.....	.5 H. Tbsp.	120
Macaroni.....	1 "	20	Grape-fruit.....	1/2 Small	150
Noodles.....	1 1/2 "	20	Huckleberries.....	3 1/2 H. Tbsp.	90
Oatmeal.....	1 "	22	Lemons.....	2 Medium	210
Rice.....	1 "	18	Muskmelon.....	1/3	300
Rye Flour.....	1 "	18	Nectarine.....	1	100
Spaghetti.....	1 1/2 "	21	Olives, Green.....	20	180
Vermicelli.....	1 1/2 "	20	Orange.....	1/2 Large	150
Wheat Flour.....	1 "	20	Peaches.....	1 1/2 Medium	150
<i>Bread and Crackers</i>			Pear.....	1 Small	100
Bread.....	1 Slice	30	Pineapple.....	.3 Slices	150
Breakfast Biscuit (Huntley & Palmer).....	3	18	Plums.....	.2 Medium	75
Cornbread.....	1 Slice	32	Raspberries.....	4 1/2 H. Tbsp.	120
Roll (Vienna).....	1/2	25	Strawberries.....	.8 "	200
Uneda Biscuit.....	3	18	Watermelon.....	Large Slice	300
Zwieback.....	1 1/3	20	<i>Dried Fruits</i>		
<i>Cooked Cereals</i>			Apples.....	.3 Small	22
"Porce".....	.5 H. Tbsp.	18	Apricots.....	.3 Large	24
Farina.....	2 1/2 "	125	Currants.....	1 1/2 Tbsp.	20
Grapenuts.....	1 1/2 "	20	Dates.....	.3	19
Hominy.....	1 1/2 "	90	Figs.....	1 Large	12
Macaroni.....	2 "	100	Prunes.....	.2 "	24
Oatmeal.....	2 1/2 "	130	Raisins.....	10 "	23
Rice.....	1/2 "	60	<i>Milk and Cream</i>		
Shredded Wheat Biscuit.....	3/4	22	Buttermilk.....	1 1/2 Tumbler	300
<i>Cooked Vegetables</i>			Cream, 16%.....	1 1/2 "	300
Artichokes.....	1 Medium	320	Cream, 40%.....	1 1/2 "	300
Beans.....			Kourmiss.....	1 1/2 "	300
(baked-canned).....	2 H. Tbsp.	75	Whole Milk.....	1 1/2	300
Beans, Lima.....	1 1/4 "	50	<i>Nuts</i>		
Beets.....	6 "	200	Almonds.....	60	90
Carrots.....	13 "	440	Brazil.....	.30	180
Okra.....	4 "	200	Chestnuts (roasted).....	15	40
Onions.....	3 "	300	Cocoanut.....	1 Slice 3x2 in.	50
Parasnips.....	4 Slices	120	Filberts.....	100	100
Peas, Green.....	3 H. Tbsp.	100	Peanuts.....	40	80
Potato (baked).....	1/2 Medium	60	Pecans.....	35	110
Potato (boiled).....	1/2 "	70	Pistachio.....	190	95
Potato (mashed).....	1 1/2 H. Tbsp.	80	Walnuts.....	30	125
Potato, Sweet (boiled).....	1/3 Medium	35			
Squash.....	2 H. Tbsp.	100			
Turnips.....	3 "	210			

\* This food list has been previously published in the Medical Clinics of North America.

In the routine treatment of these patients, a great deal of time and confusion will be saved if at each visit they will furnish a *list of the articles of food* and the approximate amounts which they have eaten during the day before. This enables the physician to tell at a glance whether his directions are thoroughly understood. If any mistakes occur under these circumstances, the patient acknowledges them freely and they may be readily corrected. Such a list, of course, is no guarantee that the patient will not transgress his limitations, but it serves to put the responsibility upon the patient. An example of such a blank, measuring  $8\frac{1}{2} \times 11$  inches, is found on Plate IV.

The *number of determinations* and the *record* which should be kept of these mild cases is indicated in the table concerning the patient C. D. C., page 105. There is a very great advantage in tabulated records of this sort, as they may be quickly interpreted, and as any other medical adviser having the case in a dispensary may become rapidly oriented by such a chart, and continue the treatment indicated without loss of time. The only addition to be made to the above chart is that there should be a space at the right for remarks, so that the progress of the disease may be watched more closely. Similar records, of course, should be kept of every patient. In the author's experience, the best results are obtained if the heads of the columns are not labeled by printed legends, but if they are filled in to suit each individual case. This makes for greater thoroughness and a more elastic system.

The *results* in these mild cases of diabetes are most gratifying. All the immediate symptoms brought on by the glycosuria, such as the thirst, the frequent voiding, marked itching, dry lips and skin, all disappear very promptly. The neuralgic pains and muscular cramps are relieved somewhat more slowly, and the former not with certainty in every case. The feeling of lassitude is replaced by one of energy, and there is a considerable gain in strength. In some cases, as in the present one, there is a gain of weight, which usually goes hand in hand with the return to a condition of full physical vigor.

(b) *Severe Cases*.—Unfortunately, such a very desirable result can be obtained only in the very mild and in the early cases of this disease; when the malady has advanced further, the urine can no longer be rendered sugar-free by restricting the diet to a carbohydrate-free regimen, but the proteins and fats, must be limited as well. In the past, we have frequently been confronted by patients from whose urine we were unable to eliminate the sugar. The most radical steps that were usually taken in this direction were to order the so-called "**green days**," containing only a very small amount of food, for two days in succession. These were very often alternated with the so-called "**oatmeal days**," on which the patient received a considerable quantity of oatmeal, butter and eggs. Such an alternation between a low diet and one containing a good deal of starch was supposed to accomplish a two-fold effect: the reduction of the glycosuria and the warding off of acidosis. The accompanying chart may give in brief the course of a case treated in this fashion. This was one of the author's cases, and it may be of interest to note that the data of 1910 were taken from those furnished by Von Noorden's clinic, and that during the winter of 1913, Von Noorden saw the case in consultation, and expressed himself as satisfied with the therapy. Two facts tailed subsequently. These are, in the first place, that the glycosuria was

PLATE IV

Diet List for M.....

For the day .....19

(Specify every article eaten, and give approximate amounts, as: 7:30 A. M., Breakfast—1 cup of coffee, bacon 2 slices, 1 egg, water 1 glass, etc. Give time of each meal. Mention all food taken between meals.)

BREAKFAST:

LUNCH:

DINNER:



never abated, and in the second place, that the acidosis constantly increased, the patient finally dying in coma. (See Table II.) Such methods of treatment are at the present of historical interest only. For the proper valuation of more recent therapy it is necessary that the poor results with former procedures should be appreciated and avoided.

TABLE 11

G. E., age 52. DIABETES MELLITUS. Progress of a case treated by "carbohydrate free," "oatmeal" and "green" diets, which finally failed to render the urine free from sugar. The life of this patient could in all probability have been indefinitely prolonged with the insulin treatment.

Date	Urine								Diet
	Vol. 24 Hrs. (c. c.)	Glucose		Diace- tic Acid	N (Grams)	NH <sub>3</sub> (Grams)	NH <sub>4</sub> -N N (Per Cent.)	NaH CO <sub>2</sub> (Grams)	
		Per Cent.	Grams						
1910									
Jul. 25	2000	0	0	0	....	...	....	..	Green day.
Aug. 2	1500	1.1	18.5	0	....	...	....	..	Carbohydrate free.
1912									
Oct. 11	3720	2.8	104.2	++++	....	2.2	....	20	Carbohydrate free.
13	2640	1.8	47.5	++++	....	0.7	....	20	2nd green day.
16	2490	3.5	87.2	++++	....	0.9	....	20	3rd oatmeal day.
18	3540	0.5	17.7	++++	10.7	0.3	2.3	20	2nd green day.
1913									
Jan. 11	3000	2.5	75.0	++++	21.8	2.6	21.8	20	2nd green day.
14	3120	2.4	74.9	++++	6.9	1.4	17.0	0	3rd oatmeal day.
16	2940	1.0	29.4	++++	14.2	0.6	4.4	20	2nd green day.
Feb. 6	3780	2.8	105.8	++++	....	...	....	0	Carbohydrate free +50 gms. of starch.
Apr. 1	2820	2.5	70.5	++++	20.7	3.5	13.9	30	2nd green day.
4	4440	2.8	124.3	++++	9.4	3.0	26.7	10	3rd oatmeal day.
5	4140	1.8	74.5	++++	16.1	3.2	16.4	30	Green day.
23	3900	3.0	117.0	++++	18.7	4.7	20.9	30	Carbohydrate free +100gms. of starch.
26	2280	2.3	52.4	++++	16.1	5.6	28.5	30	Green day.
May 10	Died in coma.								

CONSIDERATIONS GUIDING THE DIETETIC TREATMENT OF SEVERE DIABETES.—If it is claimed that the diet of the patient detailed above is incorrect there must be reasons for this statement. These are to be found in some fundamental principles that have been elaborated and applied recently; it is necessary to understand them before discussing the use of dietetic prescriptions.

*The Source of Glucose in the Body.*—When the glycosuria cannot be controlled by the simple restriction of starches in the diet as outlined under the heading of "mild or early cases" it becomes necessary to resort to more stringent dietary limitations. It is obvious that it is impossible to curtail the carbohydrates to a greater degree than has been described under the "Starch free diet, Qualitative list." There arises, therefore, the necessity for diminishing the foods which furnish glucose to the body even though they do not contain any preformed carbohydrate elements.

The following table shows the yield of glucose and fatty acid from the proteins, fats and carbohydrates:

100 Grams	Glucose Grams	Fatty Acid Grams
Protein yield in the body.....	58	46
Fats yield in the body .....	10	90
Carbohydrates yield in the body.....	100	0

It is clear from a study of this table that if glycosuria still persists after the carbohydrates have been withdrawn from the diet that the proteins must then be responsible for the formation of sugar; the fats are a negligible factor in this regard.

*Alcohol* should be mentioned in this connection. It is the one food which produces neither sugar nor fatty acid in the body while it is being katabolized. In rational amounts under suitable circumstances it is an excellent adjunct to the diabetic's food. Many alcoholic beverages contain sugar and consequently should be avoided; whiskey, brandy, sour white wine, claret and burgundy contain no sugar. Among the liquors to be avoided beer should be especially stressed, as the malt sugar seems to be particularly harmful in diabetes.

*Intarvin* (glycerol margarate) is a new form of fat which, as explained under acidosis, should give rise to sugar within the body instead of fatty acid. It has a rather disagreeable after-taste. A few years ago such a product would have been of inestimable service. Today, intelligently proportioned diets usually prevent the onset of acidosis and when coma does threaten insulin has proved itself to be the sheet-anchor of the treatment. It is regrettable that intarvin was not furnished the medical profession a few years previously, when it would have been of very great value.

*Total Metabolism.*—It is obvious that the lower the number of calories which any individual metabolizes, the less glucose will be oxidized by the body. It is generally recognized that thin persons have a lower basal metabolism than fat ones. Hence it is of distinct advantage to the diabetic to be slender. There is a limit beyond which it is not wise to proceed in reducing weight, even though the metabolism might be diminished still further. Loss of weight should be accomplished by stripping the body of needless fat and not by the sacrifice of muscular and glandular tissue. Many of these facts have often been lost sight of when diabetic patients were dieted; frequently the disease has been treated entirely to the detriment of these patients' well-being. Obesity should not be countenanced in a diabetic, neither should malnutrition.

*Proprietary "Diabetic Foods."*—The value of these should be judged entirely according to their protein, fat and carbohydrate content as determined by an analysis from a reliable source. Neither the claims of the manufacturer, the solicitations of the dealer or the advice of the saleslady are to be considered for a moment. Fortunately, at the present time the Connecticut Department of Agriculture is giving us the desired information in regard to these food products.\* No one having charge of diabetic patients should be without this pamphlet. In

\* Street, J. P.: Report of the Connecticut Agricultural experiment station on diabetic foods (to be obtained from the Connecticut Agricultural Experiment Station, New Haven, Conn.).

general the less the diabetic indulges in these proprietary food articles the more content he is.

*The Source of Acidosis in the Body.*—At the risk of repeating some of the facts previously mentioned under acidosis a brief statement concerning the dietetic factors controlling acidosis will be made. The fact is now appreciated that all foods (except alcohol) and all body tissues that may be katabolized yield fatty acid and glucose; also, that the action of the fatty acid or glucose is exactly the same whether these materials be derived from the organism itself or from the proteins, fat and carbohydrate of the diet. Glucose must be oxidized in the body in order that there shall be complete oxidation of the fatty acids to carbon dioxide and water. If sufficient glucose is not utilized the fatty acids are not completely changed to their usual end products, but remain within the body as B. oxybutyric acid, diacetic acid and acetone, ultimately to be excreted by the kidneys or by the lungs as acetone.

The table given in the previous section (page 110) indicates the yield of fatty acid and glucose from the materials digested within the body whether they be derived from the body's own tissues or the food. From this table the fatty acid: glucose, or F.A.: G. ratio may be calculated. For instance, on a diet containing 80 grams of carbohydrate, 60 of protein and 140 of fat, the F.A.: G. ratio would be calculated as follows:

	Glucose, grams	Fatty acid grams
80 grams carbohydrate yield.....	80.0	0.0
60 grams protein yield.....	34.8	27.6
140 grams fat yield.....	14.0	126.0
	128.8	153.6
$\frac{\text{F.A.}}{\text{G.}} = \frac{153.6}{128.8} = 1.2$		

Another diet analyzed in this way is:

	Glucose, grams	Fatty acid, grams
26 grams carbohydrate yield.....	26.0	0.0
34 grams protein yield.....	19.7	15.6
176 grams fat yield.....	17.6	158.4
	63.3	174.0
$\frac{\text{F.A.}}{\text{G.}} = \frac{174.0}{63.3} = 2.8$		

It is evident that in proportion to glucose one diet contains more than twice as much fatty acid as the other. What is the significance of this? Are both diets equally suitable and safe?

Under *Acidosis* it has been stated that F.A.: G. of the diet may vary a great deal without resulting in corresponding changes in acetoneuria. It has been found as high as 4:1 and higher, while the urine remained free of acetone bodies; and on the other hand on one occasion the author has noted it with a ratio of 0.74:1. The answer to such apparent discrepancies has been surmised up to the present, but has been definitely established by some experimental work of Henry B. Richardson. He found in careful calorimetric determinations that if the food materials or body tissues consumed yielded a F.A.: G. ratio above 1.5:1 acetoneuria resulted; apparent exceptions to this rule were found to be due to the fact that fat, protein or carbohydrate from the food might be assimilated or similar materials might be derived from the body substance. The only factor which can be controlled absolutely from the clinical side is the food intake; it would seem to be the safest



procedure and the most rational to prescribe diets with an F.A.:G. ratio of less than 1.5:1 if these are to be given for a long period; if for any reason a greater amount of fat is ordered the patient should be closely watched for signs of acidosis.

These facts answer our original questions. The diet with an F.A.:G. ratio of 1.2:1 is safe and will not result in acetonuria, whereas the second diet with a ratio of 2.8:1 will bring about an acidosis if the body utilizes the food completely and does not subsist in part on its own tissues.

*The Importance of Adequate Fluid Supply to the Tissues.*—The symptoms resulting from polyuria have been previously detailed; among them is dessication. This brings about a dry skin, constipation, lassitude and malaise. When it becomes very marked, in debilitated individuals or during diabetic coma, the dryness of the tissues may be one of the factors that turns the balance in the wrong direction; there has been a saying that an edematous diabetic does not die of coma. This rule may have its exceptions but they have not been common. It is obvious that when glycosuria is corrected, the voiding of large volumes of urine ceases and the proper amount of fluid is again retained by the body; some patients have to be reminded of the fact that a certain quantity of fluid is necessary in the daily diet; in emergencies the fluid may have to be forced by mouth, per rectum, intravenously and by hypodermoclysis; often the administration of liquids alone may not have the desired effect and salts of various kinds must be resorted to in order to aid in the retention of fluid within the body; sodium chloride and bicarbonate of soda are useful for this purpose. The importance of the necessity of an adequate amount of moisture in the body in routine treatment as well as during emergencies cannot be over-emphasized; if the symptoms of desiccation are constantly kept in mind the remedies are easily applied.

*The Requisite Amount of Food to Furnish Maintenance.*—The diabetic must not receive more food than he requires to maintain his health and strength; he should not receive less. The disadvantages of obesity have been discussed; on the other hand the drawbacks of debilitating the individual by depleting his glandular and muscular tissues are self-evident. It requires considerable study of each case to adjust the diet to the demands of the individual patient; age, sex, occupation, temperament, all play a rôle; when these have been carefully planned for and the diabetic consumes an exactly weighed portion of food, idiosyncrasies may appear and the diet has to be raised or lowered to meet them.

*Total Caloric Requirements* may be calculated for the patients' actual weight but it is preferable to use the normal weight. In applying this standard there will be a tendency to correct existing obesity and to have undernourished persons gain flesh, in other words, to bring about the weight most advantageous to the diabetic. The following table of normal weight for height, age and sex has been furnished by Dr. W. G. Exton, Laboratory Director of the Prudential Life Insurance Company; the figures are too high rather than too low, especially for the older ages; the averages are for persons with shoes and fully dressed.

PLATE V

AGE	MEN											WOMEN											AGE																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																										
	5 ft.	5 ft. 1 in.	5 ft. 2 in.	5 ft. 3 in.	5 ft. 4 in.	5 ft. 5 in.	5 ft. 6 in.	5 ft. 7 in.	5 ft. 8 in.	5 ft. 9 in.	5 ft. 10 in.	5 ft. 11 in.	AGE	4 ft. 8 in.	4 ft. 9 in.	4 ft. 10 in.	4 ft. 11 in.	5 ft.	5 ft. 1 in.	5 ft. 2 in.	5 ft. 3 in.	5 ft. 4 in.	5 ft. 5 in.	5 ft. 6 in.	5 ft. 7 in.	5 ft. 8 in.	5 ft. 9 in.	5 ft. 10 in.	5 ft. 11 in.	6 ft.																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																			
15	107	109	112	115	118	122	126	130	134	138	142	147	152	157	162	167	172	177	182	187	192	197	202	207	212	217	222	226	230	234	238	242	246	250	254	258	262	266	270	274	278	282	286	290	294	298	302	306	310	314	318	322	326	330	334	338	342	346	350	354	358	362	366	370	374	378	382	386	390	394	398	402	406	410	414	418	422	426	430	434	438	442	446	450	454	458	462	466	470	474	478	482	486	490	494	498	502	506	510	514	518	522	526	530	534	538	542	546	550	554	558	562	566	570	574	578	582	586	590	594	598	602	606	610	614	618	622	626	630	634	638	642	646	650	654	658	662	666	670	674	678	682	686	690	694	698	702	706	710	714	718	722	726	730	734	738	742	746	750	754	758	762	766	770	774	778	782	786	790	794	798	802	806	810	814	818	822	826	830	834	838	842	846	850	854	858	862	866	870	874	878	882	886	890	894	898	902	906	910	914	918	922	926	930	934	938	942	946	950	954	958	962	966	970	974	978	982	986	990	994	998	1002	1006	1010	1014	1018	1022	1026	1030	1034	1038	1042	1046	1050	1054	1058	1062	1066	1070	1074	1078	1082	1086	1090	1094	1098	1102	1106	1110	1114	1118	1122	1126	1130	1134	1138	1142	1146	1150	1154	1158	1162	1166	1170	1174	1178	1182	1186	1190	1194	1198	1202	1206	1210	1214	1218	1222	1226	1230	1234	1238	1242	1246	1250	1254	1258	1262	1266	1270	1274	1278	1282	1286	1290	1294	1298	1302	1306	1310	1314	1318	1322	1326	1330	1334	1338	1342	1346	1350	1354	1358	1362	1366	1370	1374	1378	1382	1386	1390	1394	1398	1402	1406	1410	1414	1418	1422	1426	1430	1434	1438	1442	1446	1450	1454	1458	1462	1466	1470	1474	1478	1482	1486	1490	1494	1498	1502	1506	1510	1514	1518	1522	1526	1530	1534	1538	1542	1546	1550	1554	1558	1562	1566	1570	1574	1578	1582	1586	1590	1594	1598	1602	1606	1610	1614	1618	1622	1626	1630	1634	1638	1642	1646	1650	1654	1658	1662	1666	1670	1674	1678	1682	1686	1690	1694	1698	1702	1706	1710	1714	1718	1722	1726	1730	1734	1738	1742	1746	1750	1754	1758	1762	1766	1770	1774	1778	1782	1786	1790	1794	1798	1802	1806	1810	1814	1818	1822	1826	1830	1834	1838	1842	1846	1850	1854	1858	1862	1866	1870	1874	1878	1882	1886	1890	1894	1898	1902	1906	1910	1914	1918	1922	1926	1930	1934	1938	1942	1946	1950	1954	1958	1962	1966	1970	1974	1978	1982	1986	1990	1994	1998	2002	2006	2010	2014	2018	2022	2026	2030	2034	2038	2042	2046	2050	2054	2058	2062	2066	2070	2074	2078	2082	2086	2090	2094	2098	2102	2106	2110	2114	2118	2122	2126	2130	2134	2138	2142	2146	2150	2154	2158	2162	2166	2170	2174	2178	2182	2186	2190	2194	2198	2202	2206	2210	2214	2218	2222	2226	2230	2234	2238	2242	2246	2250	2254	2258	2262	2266	2270	2274	2278	2282	2286	2290	2294	2298	2302	2306	2310	2314	2318	2322	2326	2330	2334	2338	2342	2346	2350	2354	2358	2362	2366	2370	2374	2378	2382	2386	2390	2394	2398	2402	2406	2410	2414	2418	2422	2426	2430	2434	2438	2442	2446	2450	2454	2458	2462	2466	2470	2474	2478	2482	2486	2490	2494	2498	2502	2506	2510	2514	2518	2522	2526	2530	2534	2538	2542	2546	2550	2554	2558	2562	2566	2570	2574	2578	2582	2586	2590	2594	2598	2602	2606	2610	2614	2618	2622	2626	2630	2634	2638	2642	2646	2650	2654	2658	2662	2666	2670	2674	2678	2682	2686	2690	2694	2698	2702	2706	2710	2714	2718	2722	2726	2730	2734	2738	2742	2746	2750	2754	2758	2762	2766	2770	2774	2778	2782	2786	2790	2794	2798	2802	2806	2810	2814	2818	2822	2826	2830	2834	2838	2842	2846	2850	2854	2858	2862	2866	2870	2874	2878	2882	2886	2890	2894	2898	2902	2906	2910	2914	2918	2922	2926	2930	2934	2938	2942	2946	2950	2954	2958	2962	2966	2970	2974	2978	2982	2986	2990	2994	2998	3002	3006	3010	3014	3018	3022	3026	3030	3034	3038	3042	3046	3050	3054	3058	3062	3066	3070	3074	3078	3082	3086	3090	3094	3098	3102	3106	3110	3114	3118	3122	3126	3130	3134	3138	3142	3146	3150	3154	3158	3162	3166	3170	3174	3178	3182	3186	3190	3194	3198	3202	3206	3210	3214	3218	3222	3226	3230	3234	3238	3242	3246	3250	3254	3258	3262	3266	3270	3274	3278	3282	3286	3290	3294	3298	3302	3306	3310	3314	3318	3322	3326	3330	3334	3338	3342	3346	3350	3354	3358	3362	3366	3370	3374	3378	3382	3386	3390	3394	3398	3402	3406	3410	3414	3418	3422	3426	3430	3434	3438	3442	3446	3450	3454	3458	3462	3466	3470	3474	3478	3482	3486	3490	3494	3498	3502	3506	3510	3514	3518	3522	3526	3530	3534	3538	3542	3546	3550	3554	3558	3562	3566	3570	3574	3578	3582	3586	3590	3594	3598	3602	3606	3610	3614	3618	3622	3626	3630	3634	3638	3642	3646	3650	3654	3658	3662	3666	3670	3674	3678	3682	3686	3690	3694	3698	3702	3706	3710	3714	3718	3722	3726	3730	3734	3738	3742	3746	3750	3754	3758	3762	3766	3770	3774	3778	3782	3786	3790	3794	3798	3802	3806	3810	3814	3818	3822	3826	3830	3834	3838	3842	3846	3850	3854	3858	3862	3866	3870	3874	3878	3882	3886	3890	3894	3898	3902	3906	3910	3914	3918	3922	3926	3930	3934	3938	3942	3946	3950	3954	3958	3962	3966	3970	3974	3978	3982	3986	3990	3994	3998	4002	4006	4010	4014	4018	4022	4026	4030	4034	4038	4042	4046	4050	4054	4058	4062	4066	4070	4074	4078	4082	4086	4090	4094	4098	4102	4106	4110	4114	4118	4122	4126	4130	4134	4138	4142	4146	4150	4154	4158	4162	4166	4170	4174	4178	4182	4186	4190	4194	4198	4202	4206	4210	4214	4218	4222	4226	4230	4234	4238	4242	4246	4250	4254	4258	4262	4266	4270	4274	4278	4282	4286	4290	4294	4298	4302	4306	4310	4314	4318	4322	4326	4330	4334	4338	4342	4346	4350	4354	4358	4362	4366	4370	4374	4378	4382	4386	4390	4394	4398	4402	4406	4410	4414	4418	4422	4426	4430	4434	4438	4442	4446	4450	4454	4458	4462	4466	4470	4474	4478	4482	4486	4490	4494	4498	4502	4506	4510	4514	4518	4522	4526	4530	4534	4538	4542	4546	4550	4554	4558	4562	4566	4570	4574	4578	4582	4586	4590	4594	4598	4602	4606	4610	4614	4618	4622	4626	4630	4634	4638	4642	4646	4650	4654	4658	4662	4666	4670	4674	4678	4682	4686	4690	4694	4698	4702	4706	4710	4714	4718	4722	4726	4730	4734	4738	4742	4746	4750	4754	4758	4762	4766	4770	4774	4778	4782	4786	4790	4794	4798	4802	4806	4810	4814	4818	4822	4826	4830	4834	4838	4842	4846	4850	4854	4858	4862	4866	4870	4874	4878	4882	4886	4890	4894	4898	4902	4906	4910	4914	4918	4922	4926	4930	4934	4938	4942	4946	4950	4954	4958	4962	4966	4970	4974	4978	4982	4986	4990	4994	4998	5002	5006	5010	5014	5018	5022	5026	5030	5034	5038	5042	5046	5050	5054	5058	5062	5066	5070	5074	5078	5082	5086	5090	5094	5098	5102	5106	5110	5114	5118	5122	5126	5130	5134	5138	5142	5146	5150	5154	5158	5162	5166	5170	5174	5178	5182	5186	5190	5194	5198	5202	5206	5210	5214	5218	5222	5226	5230	5234	5238	5242	5246	5250	5254	5258	5262	5266	5270	5274	5278	5282	5286	5290	5294	5298	5302	5306	5310	5314	5318	5322	5326	5330	5334	5338	5342	5346	5350	5354	5358	5362	5366	5370	5374	5378	5382	5386	5390	5394	5398	5402	5406	5410	5414	5418	5422	5426	5430</



Of the many methods of estimating the caloric requirements of patients only three will be given:

1. The theoretical basal metabolism for the individual (based on his or her normal weight) can be calculated from the following tables of Du Bois, and Aub and Du Bois as suggested by the department of Medicine of the University of Toronto. An increase of 20 per cent. may be allowed above the basal caloric requirement to cover the activities of a person out of bed.

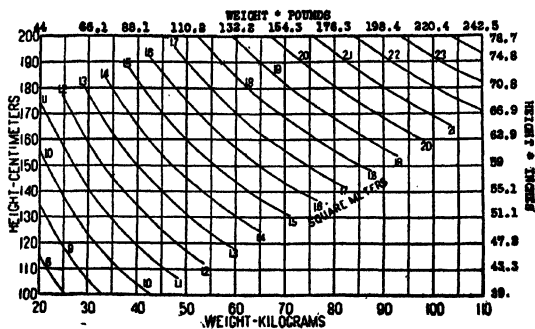


Fig. 5

## SURFACE AREA CHART (DU BOIS)

Chart for determining surface area in man in square meters. Example: Weight, 154.3 lb.; height, 70.8 in. = 1.88 sq. m.

## CALORIC REQUIREMENT PER SQUARE METRE OF BODY SURFACE (AUB-DU BOIS)

AGE	MALES		FEMALES		AGE	MALES		FEMALES	
	Cal. per		Cal. per			Cal. per		Cal. per	
Years	Hour	Day	Hour	Day	Years	Hour	Day	Hour	Day
10-12	51.5	1236	50	1200	20-30	39.5	948	37	888
12-14	50	1200	46.5	1116	30-40	39.5	948	36.5	876
14-16	46	1104	43	1032	40-50	38.5	924	36	864
16-18	43	1032	40	960	50-60	37.5	900	35	840
18-20	41	984	38	912	60-70	36.5	876	34	816

TABLE 13. METHOD FOR ESTIMATING CALORIC REQUIREMENT

2. The caloric requirements may be calculated according to the patient's weight; Joslin believes with Chittenden that 30 calories per kilo. (2.2 pounds equal 1 kilo.) suffices for any one engaged in a sedentary occupation; at rest 24 calories per kilo is enough. It is advisable to use the normal and not the actual weight as the basis for figuring.

3. Precise computations such as those attempted in sections 1 and 2 often fail to give the desired result. Certain conditions such as restlessness and likewise strenuous exercise, etc. will influence the patient's metabolism to a marked degree. Hence the caloric requirement may be judged according to the maintenance of weight at the desired level and of the sense of well being of the patient. In general according to the individual's needs 1500 to 2400 calories will be found sufficient. Small in-

active, placid persons require less food than those who are tall, of large frame, nervous in their habits and engaged in pursuits demanding a great deal of muscular exertion.

Children, because of the demands of growth and greater muscular activity, require a decidedly higher caloric adjustment than adults. A special table as devised by Holt and Fales (*American Journal Diseases of Children*, 1922 xxiv, 311) is given below. In diabetic children the protein may be given as indicated; much of the carbohydrate will have to be replaced by fat according to the principles discussed elsewhere. In some cases the author has found it advisable to give the full number of calories indicated in order to maintain proper nutrition and growth; a higher figure has not thus far been found necessary; in some instances a caloric value of 30 per cent. less than that of the table has sufficed.

TABLE 14  
THEORETICAL AVERAGE REQUIREMENTS OF HEALTHY CHILDREN (HOLT AND FALES)

AGE	Boys				Girls			
	Cal.	Fat	CH.	Prot.	Cal.	Fat	CH.	Prot.
1.....	950	35.8	115.8	35.0	940	35.4	114.7	34.5
2.....	1135	42.8	138.3	41.5	1110	41.8	135.3	40.5
3.....	1275	48.0	155.5	47.0	1230	46.4	150.0	45.0
4.....	1380	52.0	168.3	50.5	1300	49.0	158.5	47.5
5.....	1490	56.2	181.8	54.5	1410	53.2	172.0	52.0
6.....	1600	60.3	195.2	58.5	1520	57.3	184.5	56.0
7.....	1745	65.8	212.8	64.0	1660	62.6	202.2	61.0
8.....	1920	72.5	234.2	70.5	1815	68.5	221.3	66.5
9.....	2110	80.0	257.5	78.0	1990	75.0	242.8	73.0
10.....	2330	87.7	284.0	85.5	2195	82.5	268.0	80.0
11.....	2510	94.5	306.0	92.0	2520	95.0	309.8	92.5
12.....	2735	103.0	333.5	100.0	2865	108.0	349.5	105.0
13.....	3040	114.5	371.0	111.0	3210	121.0	391.7	118.0
14.....	3400	128.0	414.8	125.0	3330	125.5	406.0	122.0
15.....	3855	145.0	470.0	142.0	3235	122.5	394.5	119.0
16.....	4090	154.0	490.0	150.0	3160	119.0	385.2	116.0
17.....	3945	148.5	481.5	145.0	3060	115.5	373.2	112.0
18.....	3730	140.5	455.0	137.0	2950	111.0	360.0	108.0
Adult.....	3265	123.0	400.0	120.0	2640	100.0	322.0	97.0

Protein yields about 58 per cent. of its weight to the body as glucose and 46 per cent. as fatty acid; from this point of view it has some of the virtues as well as disadvantages of both fat and carbohydrate for the diabetic; its specific dynamic action is a little higher than that of either fat or carbohydrate, which means that there is more wasted energy, and this is to be avoided in a disease in which it is desired to maintain the level of metabolism as low as possible; on the other hand protein serves as the only food material that will replace the wear and tear of the vital tissues in the body. Provided this need is met it becomes obvious that the less protein is consumed the more economically the diabetic's diet can be adjusted.

The problem arises as to how low a protein intake can be advocated. The lowest presented for serious consideration is one containing  $\frac{2}{3}$  gram of protein per kilo. (2.2 pounds) or about 35 to 50 grams a day. The author's experience leads to the conclusion that a minimum of 1 gram per kilo. is more efficient in keeping a patient fit. It serves to prevent a protein loss in emergencies and enables the patient to store this important food product to some extent. This plan would allow 60 to 80 grams of protein in the diet per day. This very important subject cannot be properly understood without taking the matter up in some detail.

Marsh, Newburgh and Holly\* have recently shown that nitrogen equilibrium could be maintained on a very low protein, low starch diet when enough calories were provided in fat. The same diets but of lower caloric value, were used to desugarize diabetics (Table 15). It was claimed and the author also has found this to be true in occasional instances (see Table 16) that the patient's urine could be rendered sugar free on this diet when starvation had failed. The large quantity of fat offered in this diet serves to diminish the destruction of the body protein as compared with starvation and, therefore, the protein-sparing effect of the fat not only brings about a lower level of sugar metabolism (58 per cent. of protein metabolized is changed to sugar) but also lessens the inanition attendant on starvation.

TABLE 15

APPROXIMATE FOOD VALUES IN THE DIETS OF NEWBURGH AND MARSH †

Diet.	Protein.	Fat.	Carbohydrate.
No. 1 .....	20	85	15
No. 2 .....	30	140	20
No. 3 .....	35	170	30

TABLE 16

EXTRACTS FROM THE DATA OF A CASE OF DIABETES MELLITUS, A BOY WEIGHING 75 POUNDS

The high fat, low carbohydrate, and protein diet required twenty-eight days before a nitrogen balance was obtained; during this period 160 gm. of nitrogen equalizing 1,000 gm. of protein were lost to the body; it required thirty-six days to bring about a sugar-free urine; a normal blood-sugar was not brought about, although the diet was continued for a total of ninety-eight days.

Date	Urine			Food				Remarks
	Glucose, gm.	Diacetic acid	Nitrogen, gm.	Nitrogen, gm.	Protein, gm.	Fat, gm.	Carbohydrate	
May: 1								Starved for several three-day periods and not rendered sugar free.
5	54 56		11.8 15.7	3.2 3.2	20 20	89 89	15 15	Third day of diet. Seventh day of diet. Glycosuria largely due to destruction of body protein as evidenced by large amount of nitrogen in urine. Blood CO <sub>2</sub> 23.8, indicating marked acidosis.
28	9		2.1	3.2	20	89	15	Thirtieth day of diet. Nitrogen balance obtained on twenty-eighth day. No acidosis. Blood CO <sub>2</sub> 55.7; has been receiving bicarbonate of soda.
June: 3	0	0	3.8	3.2	20	89	15	Thirty-sixth day of diet. First day sugar free.

In severe cases it seems doubtful whether the maintenance obtained by these means has very many advantages. Table 16 gives extracts from the data of a boy in whom this diet attained its object in part: the urine was rendered sugar free and a nitrogen balance was obtained; but the blood sugar never became normal. During the 27 days before a nitrogen balance resulted, there was a loss of body nitrogen; 146.2 grams were

\* Marsh, P. L., Newburgh, L. H., and Holly, L. E., *Archives of Internal Medicine*, 1922, xxix, 97.

† Newburgh, L. H., and Marsh, P. L., *Archives of Internal Medicine*, 1920, xxvi, 647.

passed in the urine in excess over the intake; allowing the conservative estimate of 13.8 grams of nitrogen in the stools during this period, a loss of 160 grams of nitrogen equivalent to 1000 grams of protein is established during 27 days. This is a large amount, especially as during the previous starvation treatment there undoubtedly had been a large loss of nitrogen.

In the patients suffering with advanced diabetes (without resorting to insulin) the author has not found this diet to be more than a temporary aid when it succeeded in rendering the urine sugar free. However, this often furnishes a welcome respite. As the disease progresses and the sugar tolerance diminishes the high fat content of the diet results in acidosis which frequently terminates in coma unless the proportion of proteins, fats and carbohydrates is changed or insulin is used.

In the less severe cases the diet of Newburgh and his collaborators maintains the disease in apparent equilibrium very well. However, the author is of the opinion that those diabetics to whom he has prescribed a higher protein intake than  $\frac{2}{3}$  gram per kilo. have done better, exhibited more vitality than those kept on a minimum nitrogen intake. This can be a question of impressions only as there is no actual method of proving this point. Rubner\* apparently drew the same conclusion from his wartime observations.

Mosenthal and Harrop† showed some time ago that in the average diabetic, protein in the food results in the assimilation of considerable amounts of nitrogen, while fat and alcohol do not. This work was criticized by Marsh, Newburgh and Holly partly on the ground that the nitrogen was not determined in the feces. As a matter of fact, this chemical procedure was carried out and it was so stated in the original article. Since that time the work of Rubner, quoted previously, and that of Hoesslin ‡ and Kohn § amply bear out the statement made that in the diabetic or undernourished individual the retention of huge quantities of nitrogen is favored remarkably by protein food and much less effectively by carbohydrate, fat or alcohol.

What becomes of this retained nitrogen has been debated for some time. It would lead us too far afield to take up this problem in detail. It should be repeated that it appears that the average diabetic patient feels stronger and more energetic if he can tolerate an intake of 60 to 80 grams. There is the objection of the increased metabolism evoked by the high specific dynamic action of the proteins and their high carbohydrate yield. These are to be considered and given their due in formulating the diet in any patient, but the tendency has been to exaggerate their importance and when the diabetic's tolerance permits it the higher protein ration will yield better results as regards maintenance.

Fat in the diabetic's diet depends practically upon the amount of glucose (antiketogenic elements) in the carbohydrate and protein. These points have been discussed.

Carbohydrate assumes an entirely different position in the diabetic regime than it did before the advent of insulin. It may be said, without

\* Rubner, *Halbmonatschr. f. so z. Hyg.*, 1918, xxvi, No. 4.

† Mosenthal, H. O., and Harrop, G. A., *Archives of Int. Med.*, 1918, xxii, 750.

‡ Hoesslin, H., *Arch. f. Hyg.*, 1918, lxxxviii, 147.

§ Kohn, K., *Wien. klin. Woch.*, 1919, xxii, 135.

fear of contradiction, that no diet is palatable over long periods without at least 50 grams of carbohydrate. The quantity allowed must of course be adjusted to the patient's tolerance and more allowed if possible; if 50 grams are not tolerated insulin should be resorted to. The importance of starch in the diet in order to prevent acidosis has been detailed.

*Prescribing Weighed Diets.*—Diets of any desired composition may be calculated from the accompanying analyses grouped from: Atwater and Bryant, *The Chemical Composition of American Food Materials*, Bull. 28, U. S. Dept. Agriculture; Joslin, *The Treatment of Diabetes Mellitus*; Locke, *Food Values*. These works may be consulted for greater details. In the second section a system of diets is given which has proved itself of value in the treatment of all classes of cases, hospital, dispensary or private practice, when weighing of food is indicated.

*Composition of Foods.*—The foods are grouped according to their protein, fat and carbohydrate content.

## VEGETABLES AND FRUITS

3 per cent. Carbohydrate, 1 per cent. Protein

	Prot.	Fat	CH		Prot.	Fat	CH
Artichokes, canned.....	.8		5.0	Mushrooms.....	3.5	.4	6.8
Asparagus cooked.....	2.1	3.3	2.2	Olives, ripe.....	1.4	21.0	3.5
Asparagus, fresh.....	1.8	.2	3.3	Pickles, canned.....	.7	.1	3.6
Asparagus tips.....				Pickles, dill.....	.5	.3	2.7
Beans, string fresh.....	2.1	.3	6.9	Pickles, mixed.....	1.1	.4	4.0
Beans, wax canned.....	1.0	.1	3.1	Radishes.....	1.3	.1	5.8
Beet Greens, cooked.....	2.2	3.4	3.2	Sauerkraut.....	1.7	.5	3.8
Brussels sprouts.....	1.5	.1	3.4	Sorrel.....			3.0
Cabbage.....	1.6	.3	5.6	Spinach.....	2.1	.3	3.2
Cauliflower.....	1.8	.5	4.7	String beans, coked.....	.8	1.1	1.9
Celery.....	1.1	.1	3.3	String beans, canned.....	1.1	.1	3.3
Cucumbers.....	.8	.2	3.1	Swiss chard.....			
Egg plant.....	1.2	.3	5.1	Tomatoes, fresh.....	.9	.4	3.9
Endive.....	1.0		2.6	Tomatoes, canned.....	1.2	.2	4.0
Kohlrabi.....	2.0	.1	5.5	Water cress.....	0.7	.5	3.7
Leeks.....	1.2	.5	5.8				
Lettuce.....	1.2	.3	2.9	Rhubarb.....	.6	.7	3.6
Marrow.....	0.1	.2	2.6				

## VEGETABLES, FRUITS AND CEREALS

10 per cent. Carbohydrate, 1 per cent. Protein

	Prot.	Fat	CH		Prot.	Fat	CH
Beets.....	1.6	.1	9.7	Cranberries.....	.4	.6	9.9
Carrots.....	1.1	.4	9.3	Currants.....	1.5		12.8
Dandelion, green.....	2.4	1.0	10.6	Gooseberries.....	0.4		12.0
Green peas, canned.....	3.6	.2	10.0	Grapefruit, soluble portion.....		.7	6.0
Horse radish.....	1.4	.2	10.5	Lemons.....	1.0		8.5
Okra.....	1.0	.2	7.4	Muskmelon, edible portion.....	.6		9.3
Olives.....	.8	20.2	8.5	Oranges, edible portion.....	.8	.2	11.6
Onions, cooked.....	1.2	1.8	4.9	Peaches, edible portion.....	.7	.1	9.4
Onions, fresh.....	1.6	.3	9.9	Pineapple, edible portion.....	.4	.3	9.7
Parsnips.....	1.6	.5	13.5	Raspberries.....	1.0		12.6
Pumpkin.....	.8	.2	6.7	Strawberries.....	1.0	.6	7.4
Squash.....	1.4	.5	9.0	Watermelon, edible portion.....	.4	.2	6.7
Turnip.....	1.3	.2	8.1				
Apples.....	.3	.3	10.8	Farina, boiled.....	6.8	2.0	11.5
Blackberries.....	1.3	1.0	10.9	Oatmeal, boiled.....	2.8	.5	11.5



## VEGETABLES, FRUITS AND CEREALS

20 per cent. Carbohydrate, 3 per cent. Protein

	Prot.	Fat	CH		Prot.	Fat	CH
Artichokes, fresh	2.6	.2	16.7	Apricots	1.1		13.4
Beans, canned baked	6.9	2.5	19.6	Bananas	1.3	.6	22.0
Beans, home-made baked	7.2	8.5	21.9	Blueberries	.6		13.0
Corn, green edible portion	3.1	1.1	19.7	Cherries	1.0	.8	16.7
Corn, green canned	2.8	1.2	19.0	Huckleberries	.6	.6	16.6
Green peas, fresh	7.0	.5	16.9	Nectarines	.6		14.8
Lima beans	7.1	.7	22.0	Pears	.6	.5	14.1
Macaroni, cooked	3.0	1.5	15.8	Plums, edible portion	1.0		20.1
Potatoes, boiled	2.5	.1	20.9	Hominy cooked	2.2	.2	17.8
Potatoes, mashed and creamed	2.6	3.0	17.8				
Rice, boiled	2.8	.1	24.4				

## BREADS

55 per cent Carbohydrate, Protein 10 per cent., Fat 2 per cent.

	Prot.	Fat	CH		Prot.	Fat	CH
Bread				Bread			
Biscuit "home-made"	8.7	2.6	55.3	Rolls, plain	9.7	4.2	59.9
Buns	6.3	6.5	57.3	Rolls, Vienna	8.5	2.2	56.5
Corn	7.9	4.7	46.3	Rye	9.0	.6	53.2
"Gluten" as purchased	9.3	1.4	49.8	Toasted	11.5	1.6	61.2
Graham	8.9	1.8	52.1	White	9.2	1.3	53.1
Rolls, French	8.5	2.5	55.7	Whole wheat	9.7	.9	49.7

## CRACKERS AND UNCOOKED CEREALS

75 per cent. Carbohydrate, Protein 10 per cent.

	Prot.	Fat	CH		Prot.	Fat	CH
Force	10.6	1.1	74.0	Pretzels	9.7	3.9	72.8
Grapenuts	11.5	.6	75.0	Saltines	10.6	12.7	68.5
Puffed Rice	6.7	0.4	80.0	Soda cracker	9.8	9.1	73.1
Toasted Cornflakes			81.0	"Uneda" cracker	10.1	8.8	70.0
Triscuit	11.0	1.4	75.0	1 cracker 7 gm.	0.7	0.5	5.0
Graham crackers	10.0	9.4	73.8	Water cracker	11.7	5.0	75.7
Oatmeal crackers	11.8	11.1	69.0	"Zephyrs"	9.8	9.1	73.1
Oyster crackers	11.3	10.5	70.5	1 cracker	1.0	.9	7.3
Pilot bread	11.1	5.0	74.2	Zwieback	9.8	9.9	73.5

## MEAT AND FISH

1 per cent. Protein, 20 per cent. Fat

	Prot.	Fat		Prot.	Fat
Beef, boiled			Mutton, boiled lean	23.2	3.4
Beef, corned, edible portion	15.6	26.2	Mutton chop, lean	22.6	4.5
Beef kidney, edible portion	16.6	4.8	Mutton roast, edible portion	25.0	22.6
Beef roast	22.3	28.6	Pork chop, edible portion	16.4	32.0
Beef steak, round cooked lean	27.6	7.7	Pork roast	28.4	10.0
Beef steak, tenderloin broiled	23.5	20.4	Squab (pigeon) meat, except giblets	18.5	23.8
Beef tongue, fresh edible portion	18.9	9.2	Turkey, roast, edible portion	27.8	18.4
Capon, cooked, edible portion	27.0	11.5			
Chicken, edible portion broilers	21.5	2.5	Butter fish	18.0	11.0
Chicken, edible portion fowl	19.3	16.3	Eels, edible portion	17.8	7.9
Duck meat, except breast and giblets	17.4	26.1	Halibut, smoked	20.7	15.0
Goose, young, edible portion	16.3	36.2	Herring, smoked, edible portion	20.5	8.8
Guinea Hen meat, except giblets	23.4	6.5	Mackerel, edible portion	18.7	7.1
Ham, fresh edible portion	15.7	33.4	Mackerel, salt dressed	17.3	26.4
Ham, smoked edible portion	16.5	38.8	Salmon, canned	21.8	12.1
Ham, smoked boiled	20.2	22.4	Salmon, edible portion	22.0	12.8
Ham, smoked, fried	22.2	33.2	Sardines, canned	21.2	12.7
Lamb chops, broiled, edible portion	21.7	29.9	Shad, edible portion	18.8	9.5
Lamb roast	19.7	12.7			

## FISH

20 per cent. Protein, 3 per cent. Fat

	Prot.	Fat		Prot.	Fat
Bass, Black, edible portion . . . . .	20.6	1.7	Halibut, edible portion . . . . .	18.6	5.2
Bass, Sea, edible portion . . . . .	19.8	.5	Perch, yellow, edible portion . . . . .	18.7	.8
Bass, Striped, edible portion . . . . .	18.6	2.8	Pollock, edible portion . . . . .	21.6	.8
Blue fish, edible portion . . . . .	19.4	1.2	Porgy, edible portion . . . . .	18.6	5.1
Blue fish, cooked, edible portion . . . . .	25.9	4.5	Shad, . . . . .	20.9	3.8
Cod fish, fresh, edible portion . . . . .	16.5	.4	Smelt, edible portion . . . . .	17.6	1.8
Cod, salt, edible portion . . . . .	25.4	.3	Trout, edible portion . . . . .	19.2	2.1
Flounder, edible portion . . . . .	14.2	.6	Weak fish, edible portion . . . . .	17.8	2.4
Haddock, fresh, edible portion . . . . .	17.2	.3	White fish, edible portion . . . . .	22.9	6.5
Haddock, smoked . . . . .	23.3	.2			

## CHEESE

25 per cent. Protein, 35 per cent. Fat

	Prot.	Fat	CH		Prot.	Fat	CH
American pale . . . . .	28.8	35.9	.3	Limburger . . . . .	23.0	29.4	.4
American red . . . . .	29.6	38.3		MacLaren's Nippy . . . . .	26.9	38.6	
Camembert . . . . .	21.0	21.7		Neuchatel . . . . .	18.7	27.4	1.5
Cottage . . . . .	20.9	1.0	4.3	Pineapple . . . . .	20.9	38.9	2.6
Crown brand cream . . . . .	5.2	58.0	2.2	Roquefort . . . . .	22.6	29.5	1.8
Fromage de Brie . . . . .	15.9	21.0	1.4	Swiss . . . . .	27.6	34.9	1.3
Full cream . . . . .	25.9	33.7	2.4	Star brand cream . . . . .	12.7	47.3	
Liederkranz . . . . .	16.3	26.4		Stilton . . . . .	23.9	38.9	

## MILK AND CREAM

	Prot.	Fat	CH		Prot.	Fat	CH
Butter milk . . . . .	2.8	2.1	5.4	Milk, whole . . . . .	3.0	0.5	4.8
Koumiss . . . . .	8.8	8.3	54.1	Cream as purchased . . . . .	2.5	18.5	4.5
Milk, condensed, sweetened . . . . .				Cream, average . . . . .	3.7	25.7	3.6
Milk, condensed, unsweetened . . . . .	9.6	9.3	11.2	Cream, heavy . . . . .	2.2	36.2	2.9
("evaporated cream") . . . . .	3.4	0.3	5.1	Cream, thick . . . . .	1.5	56.1	2.3
Milk, skimmed . . . . .	3.3	4.0	5.0	Cream, whipped . . . . .	33.4	23.2	3.2

## OILS AND FATS

	Prot.	Fat		Prot.	Fat
Butter . . . . .	1.0	85.0	Peanut oil . . . . .	85-100	
Oleomargarine . . . . .	1.2	83.0	Wesson oil . . . . .		
Olive oil . . . . .		100.0	Mazola . . . . .		
			Other fats and oils . . . . .		

## BACON

	Prot.	Fat		Prot.	Fat
Cooked medium . . . . .	16.0	40.0	Smoked edible portion . . . . .	10.5	64.8

## GELATIN

	Prot.	Fat		Prot.	Fat
Cooked . . . . .	6.6	0	Uncooked . . . . .	91.4	0.1

## EGGS

	Prot.	Fat		Prot.	Fat
Edible portion . . . . .	13.4	10.5	1 yolk, boiled, 18 grams . . . . .	2.9	6.0
Boiled whites . . . . .	12.3	.2	1 white, boiled, 32 grams . . . . .	4.2	.1
Boiled yolks . . . . .	15.7	33.3	1 egg, boiled, 50 grams . . . . .	6.6	6.0

## FOODS WITHOUT FOOD VALUE

Agar agar,  
Broth, skimmed,  
Clear coffee,  
Clear tea,

Cocoa shells,  
Cracked cocoa,  
Mineral oil,  
Starch free bran biscuits,

Starch free bran cereal,  
Thrice boiled vegetables.

**WEIGHED DIETS FOR USE IN CASES OF DIABETES MELLITUS NOT COMPLICATED BY ACIDOSIS.**—The following weighed diets are designed to meet the need of diabetics as they present themselves in medical practice.

1. The protein content is approximately equivalent to 1 gram per kilo.

2. The fats are given in such amounts that the fatty acid glucose ratio is about 1.2:1, a ratio adequate to prevent acidosis.

3. The carbohydrates are not reduced to the absolute minimum but are allowed in moderate amounts; this permits of a much greater variety in the choice of food and consequently a more palatable diet; if glycosuria does appear with this allowance of carbohydrates it is best to resort to insulin to right the situation.

4. When diets greater than 2500 calories can be taken without the presence of sugar in the urine usually a qualitative diet suffices and there is no longer a necessity of weighing the food.

5. For a summary of these diets and a chart that serves to guide the patient see Table 17, Plate VI.

The composition of these diets is as follows:

	Protein, Grams	Fat, Grams	Carbohydrate, Grams	Total Calories
Diet 1.....	15	35	20	469
Diet 2.....	30	70	40	938
Diet 3.....	45	105	60	1407
Diet 4.....	60	140	80	1876
Diet 5.....	75	175	100	2345

The food having no food value may be used as desired in addition to articles of diet given. It is important that the patient understands this.

The groups referred to are those in the series of tables given on pages—under the heading of "Composition of Foods."

## DIABETIC DIET No. 1

Protein 15 grams; fat 35 grams; carbohydrate 20 grams; total calories 469

	Grams	Protein	Fat	CH
<i>Breakfast:</i> Cereal or fruit 10 per cent. CH group....	70	0.7		7.0
Cream 20 per cent.....	30	1.1	6.0	1.1
<i>Lunch:</i> Vegetables 3 per cent. CH group.....	200	2.0		6.0
Butter .....	12	.1	10.2	
<i>Supper:</i> Meat group.....	45	9.0	9.0	
Vegetables 3 per cent. CH group.....	200	2.0		6.0
Butter .....	12	.1	10.2	
		15.0	35.4	20.1

## DIABETIC DIET No. 2

Protein 30 grams; fat 70 grams; carbohydrate 40 grams; total calories 938

<i>Breakfast:</i> Fruit 10 per cent. CH group.....	100	1.0		10.0
Cereal 10 per cent. CH group.....	100	1.0		10.0
Cream 20 per cent.....	60	2.2	12.0	2.2
Butter .....	15	.2	12.8	
<i>Lunch:</i> Vegetables 3 per cent. CH group.....	100	1.0		3.0
Vegetables or fruit 10 per cent. CH group	90	.9		9.0
Butter .....	15	.2	12.8	
<i>Supper:</i> Meat group.....	100	20.0	20.0	
Vegetables 3 per cent. CH group.....	200	2.0		6.0
Butter .....	15	.2	12.8	
		28.7	70.4	40.2

# DIABETIC DIETS

121

## DIABETIC DIET No. 3

Protein 45 grams; fat 105 grams; carbohydrate 60 grams; total calories 1407

<i>Breakfast:</i>	Fruit 10 per cent. CH group.....	100	1.0		10.0
	Cereal 10 per cent. CH group.....	100	1.0		10.0
	Cream 20 per cent.....	60	2.2	12.0	2.2
	Butter .....	15	.2	12.8	
<i>Lunch:</i>	Meat group.....	120	24.0	24.0	
	Butter .....	15	.2	12.8	
	Vegetables 3 per cent. CH group.....	100	1.0		3.0
	Vegetables or fruit 10 per cent. CH group	90	.9		9.0
	Olive oil.....	15		15.0	
<i>Supper:</i>	Vegetables 3 per cent. CH group.....	200	2.0		6.0
	Butter .....	15	.2	12.8	
	Egg .....	50	6.6	6.0	
	Cream 20 per cent.....	30	1.1	6.0	1.1
	Bread .....	30	2.8	.4	15.9
			44.3	107.8	58.3

## DIABETIC DIET No. 4

Protein 60 grams; fat 140 grams; carbohydrate 80 grams; total calories 1876

<i>Breakfast:</i>	Fruit 10 per cent. CH group.....	100	1.0		10.0
	Cereal 10 per cent. CH group.....	100	1.0		10.0
	Egg .....	50	6.6	6.0	
	Bacon cooked.....	30	4.8	12.0	
	Butter .....	20	.2	17.0	
	Cream 20 per cent.....	60	2.2	12.0	2.2
<i>Lunch:</i>	Meat group.....	100	20.0	20.0	
	Vegetables 3 per cent. CH group.....	100	1.0		3.0
	Vegetables or fruit 10 per cent. CH group	100	1.0		10.0
	Butter .....	20	.2		
	Olive oil.....	15		15.0	
	Cream 20 per cent.....	30	1.1	6.0	1.1
<i>Supper:</i>	Eggs 2.....	100	13.2	12.0	
	Vegetables 3 per cent. CH group.....	100	1.0		3.0
	Vegetables 20 per cent. CH group.....	100	3.0		20.0
	Butter .....	20	.2	17.0	
	Cream 20 per cent.....	30	1.1	6.0	1.1
	Bread .....	30	2.8	.4	15.9
			60.4	140.4	76.3

## DIABETIC DIET No. 5

Protein 75 grams; fat 175 grams; carbohydrate 100 grams; total calories 2,345

		Grams	Protein	Fat	CH
<i>Breakfast:</i>	Fruit 10 per cent. CH group.....	100	1.0		10.0
	Cereal 10 per cent. CH group.....	100	1.0		10.0
	Egg 1.....	50	6.6	6.0	
	Bacon .....	30	4.8	12.0	
	Butter .....	30	.3	25.5	
	Cream 20 per cent.....	60	2.2	12.0	2.2
<i>Lunch:</i>	Meat group.....	100	20.0	20.0	
	Vegetables 3 per cent. CH group.....	100	1.0		3.0
	Vegetables or fruit 10 per cent. CH group	100	1.0		10.0
	Bread .....	30	2.8	.4	15.9
	Butter .....	30	.3	25.5	
	Olive oil.....	15		15.0	
	Cream 20 per cent.....	30	1.1	6.0	1.1
<i>Supper:</i>	Meat group.....	100	20.0	20.0	
	Vegetables 3 per cent. CH group.....	100	1.0		3.0
	Vegetables 20 per cent. CH group.....	100	3.0		20.0
	Butter .....	20	.2	17.0	
	Bread .....	30	2.8	.4	15.9
	Cream 20 per cent.....	30	1.1	6.0	1.1
	Milk .....	200	6.6	8.0	10.0
			76.8	173.8	102.2

**WEIGHED DIETS FOR CASES OF DIABETES MELLITUS EXHIBITING ACIDOSIS.** These diets have a very low fat content and a comparatively liberal allowance of starchy food. In order to bring about utilization and consequent benefit from the carbohydrates, Insulin will have to be resorted to in most patients. These diets have the following composition:

	Protein grams	Fat grams	Carbohydrate grams	Total Calories
<i>Diet 1</i> .....	30	4	20	242
<i>Diet 2</i> .....	45	5	60	477
<i>Diet 3</i> .....	65	5	100	723

#### ACIDOSIS DIET No. 1

Protein 30 grams; fat 4 grams; carbohydrate 20 grams; total calories 242

	Grams	Protein	Fat	CH
<i>Breakfast:</i> Vegetables 3 per cent. CH group.....	100	1.0		3.0
Skimmed milk.....	100	3.4	0.3	5.1
<i>Lunch:</i> Vegetables 3 per cent. CH group.....	100	1.0		3.0
Fish 3 per cent. fat group.....	100	20.0	3.0	
<i>Supper:</i> Vegetables 3 per cent. CH group.....	100	1.0		3.0
Skimmed milk.....	100	3.4	0.3	5.1
		29.8	3.6	19.2

#### ACIDOSIS DIET No. 2

Protein 45 grams; fat 5 grams; carbohydrate 60 grams; total calories 477

	Grams	Protein	Fat	CH
<i>Breakfast:</i> Fruits 10 per cent. CH group.....	100	1.0		10.0
Cereal 10 per cent. CH group.....	100	1.0		10.0
Skimmed milk.....	200	6.8	0.6	10.2
<i>Lunch:</i> Fish 3 per cent. fat group.....	100	20.0	3.0	
Vegetables 3 per cent. CH group.....	100	1.0		3.0
Skimmed milk.....	100	3.4	0.3	5.1
<i>Supper:</i> Fruits 10 per cent. CH group.....	120	1.2		12.0
Gelatin .....	80	5.3		
Skimmed milk.....	200	6.8	0.6	10.2
		46.5	4.5	60.5

#### ACIDOSIS DIET No. 3

Protein 65 grams; fat 5 grams; carbohydrate 100 grams; total calories 723

	Grams	Protein	Fat	CH
<i>Breakfast:</i> Fruits 20 per cent. CH group.....	100	1.0		20.0
Cereal 10 per cent. CH group.....	100	1.0		10.0
Skimmed milk.....	200	6.8	0.6	10.2
<i>Lunch:</i> Fish 3 per cent. fat group.....	100	20.0	3.0	
Vegetables 3 per cent. CH group.....	100	1.0		3.0
Fruit or vegetables 20 per cent. CH group	100	3.0		20.0
Skimmed milk.....	100	3.4	0.3	5.1
<i>Supper:</i> Fish 3 per cent. fat group.....	75	15.0	0.2	
Vegetables 20 per cent. CH group.....	100	3.0		20.0
Gelatin .....	80	5.3		
Skimmed milk.....	200	6.8	0.6	10.2
		66.3	4.7	98.5

**THE TREATMENT OF SEVERE CASES.**—The application of the principles outlined to actual cases may follow various schemes; all of them are roughly divisible into three stages: desugarization, maintenance and adjustment. This implies that the urine should be rendered sugar free, the blood sugar reduced to normal and acidosis eliminated; that these

# PLATE VI

TABLE 17

## SUMMARY OF DIETS FOR USE IN DIABETES MELLITUS

This Table printed on heavy paper and folded in the centre makes a convenient form for dietary prescriptions; it obviates the necessity for the patient or nurse to calculate the quantity of food every day.

Vegetables and Fruits 10% CH, 1% prot.	Vegetables, Fruits and Cereals 10% CH, 1% prot.	Vegetables, Fruits and Cereals 20% CH, 8% prot.	Meat and Fish 20% prot. 20% fat	Fish 20% prot. 3% fat
Artichokes canned Asparagus Beans string Beans wax Beet greens Brussels sprouts Cabbage Cauliflower Celery Cucumbers Egg plant Endive Kohlrabi Lentils Lettuce Marrow Mushrooms Olives ripe Pickles Radishes Sauerkraut Sardines Spinach Swiss chard Tomatoes Water cress	Beets Carrots Dandelion greens Green peas canned Horse radish Okra Olives green Onions Parsnips Pumpkin Squash Turnip  Apples Blackberries Cranberries Currants Gooseberries Grapefruit edible part Lemons Muskmelon Oranges Peaches Pineapple Raspberries Strawberries Watermelon  Farina boiled Oatmeal boiled	Artichokes fresh Beans baked Beans baked canned Corn green Corn green canned Green peas fresh Lima beans Macaroni cooked Potatoes Rice boiled  Apricots Bananas Blueberries Cherries Huckleberries Nectarines Pears Plums  Hominy cooked	Beef boiled Beef corned Beef Kidney Beef roast Beef steak Beef tongue Capon Chicken broilers Chicken fowl Duck Geese Guinea Hen Ham Lamb chops Lamb roast Mutton chop Mutton Pork chop Pork roast Squab Turkey Butter fish Eels Halibut smoked Herring smoked Mackerel fresh Mackerel salt Salmon canned Salmon fresh Sardines canned Shad	Bass black Bass sea Bass striped Blue fish Cod fish fresh Cod fish salt Flounder Haddock Halibut Perch yellow Pollock Porgy Shad roe Smelt Trout Weak fish White fish

Foods Without Food Value  
May Be Taken As Desired

Weight equivalents:  
30 grams = 1 ounce

1 egg weighs 50 grams

Household measures:

1 flat teaspoonful = 5 grams

1 flat tablespoonful = 15 grams

1 heaping tablespoonful, cut meat or fish = 30 grams

1 water glass full = 250 grams

DIET IN GRAMS						Vegetables 3% CH	Vegetables 10% CH	Vegetables 20% CH	Fruit 10% CH	Cereal 10% CH	Meat and fish 20% Fat	Fish 3% Fat	Butter	Cream 20%	Eggs	Olive oil	Bread	Bacon Cooked	Milk	Skimmed Milk	Gelatine	Fruit 20% CH
Diabetic Diet	1	20	15	35	460	...	...	...	70	...	...	...	12	30	...	...	...	...	...	...	...	...
		...	...	...	...	200	...	...	...	...	45	...	12	...	...	...	...	...	...	...	...	...
		...	...	...	...	200	...	...	...	...	...	...	12	...	...	...	...	...	...	...	...	...
	2	40	30	70	938	...	90	...	100	100	...	...	15	60	...	...	...	...	...	...	...	...
		...	...	...	...	100	...	...	...	...	100	...	15	...	...	...	...	...	...	...	...	...
		...	...	...	...	200	...	...	...	...	...	...	15	...	...	...	...	...	...	...	...	...
	3	60	45	105	1407	...	90	...	100	100	...	...	15	60	...	15	...	...	...	...	...	...
		...	...	...	...	100	...	...	...	...	120	...	15	30	...	...	...	...	...	...	...	...
		...	...	...	...	200	...	...	...	...	...	...	15	30	...	50	...	...	...	...	...	...
	4	80	60	140	1876	...	...	...	100	100	...	...	20	60	50	...	...	...	...	...	...	...
		...	...	...	...	100	...	...	...	...	100	...	20	30	...	15	30	...	...	...	...	...
		...	...	...	...	100	...	100	...	...	...	...	20	30	100	...	...	...	...	...	...	...
	5	100	75	175	2345	...	...	...	100	100	...	...	30	60	50	...	...	...	...	...	...	...
		...	...	...	...	100	...	...	...	...	100	...	30	30	...	15	30	...	...	...	...	...
		...	...	...	...	100	...	100	...	...	...	...	20	30	...	...	30	...	200	...	...	...
Acidosis Diet	6	20	30	4	242	...	...	...	...	...	...	100	...	...	...	...	...	...	...	100	...	...
		...	...	...	...	100	...	...	...	...	...	...	...	...	...	...	...	...	...	100	...	...
		...	...	...	...	100	...	...	...	...	...	...	...	...	...	...	...	...	...	100	...	...
	7	60	45	5	477	...	...	...	100	100	...	...	...	...	...	...	...	...	...	200	...	...
		...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	100	...	...
		...	...	...	...	...	...	...	120	...	...	...	...	...	...	...	...	...	...	200	80	...
	8	100	65	5	723	...	...	...	100	...	...	...	...	...	...	...	...	...	...	200	...	100
		...	...	...	...	100	...	...	...	...	...	...	...	...	...	...	...	...	...	100	...	...
		...	...	...	...	...	...	...	...	...	...	...	...	75	...	...	...	...	...	200	80	...

Foods without food value as desired with any diet.



conditions are maintained while the diet is brought to a level which provides an adequate amount of nourishment; and that the diet is adjusted as the carbohydrate tolerance of the patient increases or diminishes or as there is an excessive gain or loss of weight.

*Desugarization.*—There are many procedures that may be resorted to; which one of them is recommended depends somewhat on the presence or absence of acidosis; the urgency of preparing for operation or putting the patient in the best condition to combat infection or gangrene; the call to preserve strength in very weak and emaciated individuals, etc. The physician's judgment must dictate the preferable method under the circumstances; some of these methods of desugarization are:

1. A diet below the caloric requirement of the patient is chosen; such a diet as is represented in Diabetic Diets, 1, 2 or 3 (pages 120, 121) or Table 17. The glycosuria is determined in consecutive 24-hour specimens until it ceases to diminish. If it does not disappear and the blood sugar return to normal a still lower diet is ordered and the steps repeated until desugarization is complete. It may be necessary to resort to starvation as detailed under 2. This mode of desugarizing the diabetic requires longer than starvation but it conserves the body tissues of the patient to a greater extent.

2. When the disposition to acidosis is not marked, starvation may be resorted to immediately. This consists in allowing foods without nutritional value. There are: Coffee, tea, cocoa from cocoa shells or cracked cocoa (all without cream, milk or sugar); skimmed broth; starch-free bran biscuits or cereal; agar agar; thrice boiled green vegetables; mineral oil; alcohol may be allowed to those accustomed to it (alcohol produces neither sugar nor fatty acids and may thus be regarded as an ideal food for the diabetic). These food restrictions are continued until "desugarization" is achieved.

There are many physicians who believe that starvation should not be advised for more than three consecutive days, when it may be alternated with a low caloric diet, to be resumed again after an interval of three or four days if necessary.

3. In severe cases exhibiting a marked degree of acidosis the steps mapped out by Joslin are the safest; these are:

The continuance of the patient's usual diet with these successive restrictions:

- (a) The elimination of all fats from the diet for two days—this does away with the main source of acid substances whose deficient oxidation is responsible for the acidosis.

- (b) The restriction of the protein containing foods for two days—thereby the remaining dietary factors producing acetone bodies are removed and also some of those which form glucose.

- (c) Finally the starches are halved every day—this step brings the diet to the starvation point, when all the sugar and acetone substances must be derived from the body's own tissues—further details of the "starvation treatment" are explained in the preceding section.

4. The patient may be immediately given an approximate maintenance diet (such as diets No. 4 and 5, page 121, also Table 17) and desugarization aided by the administration of insulin.

*Maintenance.*—After desugarization is complete the diet is gradually increased until a maintenance level has been reached. Various conceptions regarding this have been explained; the diets we have



been using in this connection are diets No. 4 and No. 5 (page 121). If the patient can not be kept upon a diet of this sort while free from sugar in the urine recourse must be had to insulin.

*Adjustment.*—It is obvious that from time to time nearly all diabetics require an adjustment of diet or insulin administration to the ever changing carbohydrate tolerance. This may grow worse or improve, it may change remarkably for short periods with nervous upsets or minor infections such as coryza or digestive disturbances. It is impossible to give examples of all of these. One very interesting instance may suffice. This case report, Table 18, besides illustrating the change that may occur in carbohydrate tolerance also serves to show that in some patients the power of the body to utilize glucose may improve in a very remarkable way while insulin therapy is employed.

In supervising obstinate cases of diabetes mellitus the physician is often confronted with the problem of obtaining a normal blood sugar and a sugar free urine in all cases. These are desirable if they can be achieved and maintained. It is undoubtedly true that the majority of diabetics do poorly while they exhibit glycosuria; very severe cases that

TABLE 18  
CASE OF DIABETES MELLITUS—FEMALE—AGE 36

There is marked improvement in the carbohydrate tolerance while insulin treatment is carried out. Note the reduction in insulin while the urine remains sugar free.

Date	Glucose Urine, grams	Diet				Insulin Units
		Protein, grams	Fat, grams	CH. grams	Total. Calories	
Dec. 13. ....	11.2	60	140	80	1876	30
14. ....	16.9	60	140	80	1876	35
15. ....	10.0	60	140	80	1876	45
16. ....	5.0	60	140	80	1876	45
20. ....	0.0	60	140	80	1876	45
26. ....	4.7	60	140	80	1876	30
Jan. 3. ....	0.0	60	140	80	1876	40
12. ....	0.0	60	140	80	1876	25
19. ....	0.0	60	140	80	1876	15
26. ....	0.0	60	140	80	1876	10

are receiving heavy doses in insulin (60 units or more per day) apparently are an exception to this rule. It may be that the glucose utilizing power has been completely destroyed in them and that they do well as long as they have insulin digesting at least a portion of their starchy food. There is considerable danger of hypoglycemic shock if higher doses of insulin are employed. In such instances I have found that the glycosuria apparently is not detrimental. One patient of this kind has had a glycosuria for nearly a year and a half and is doing splendidly; he has the appearance of a normal individual and accomplishes as much work as his neighbors.

At present the idea is generally accepted that a diabetic should have a normal blood sugar. It is undoubtedly true that the injured pancreatic function is spared to the utmost under these circumstances and the chances for a recovery of some of the lost carbohydrate tolerance are favored thereby. However, there is no proof at hand that an increase of glycemia above the accepted normal levels diminishes the power of the body to utilize glucose or that a hyperglycemia favors the development of diabetic complications, provided the urine remains sugar free. Because of this state of the whole problem the author has not been insistent on maintaining a normal blood sugar where it has entailed a great

sacrifice on the patient's part; such cases with hyperglycemia have done exceedingly well and their condition has been satisfactory.

*Exercise* is one of the best adjuncts in increasing carbohydrate tolerance. It is a wise attitude to take to tell patients that they are only dietary invalids, that all exercise and all other pleasures may be indulged in as by any normal person. The diabetic should take some physical exercise every day. The amount must be adjudged in each case. Excessive fatigue should not be sought for. A feeling of "tiredness" as the result of physical effort is a welcome one. It induces a sound, healthy sleep, of which the diabetic should have a full measure.

**The Use of Insulin in Diabetes Mellitus.**—Insulin is the name given to an extract derived from the Islands of Langerhans of the pancreas; on hypodermic injection it corrects the metabolic disturbances occurring in diabetes mellitus; it is the only means of treating this condition when dietetic regulation fails to control the disease.

Dr. F. G. Banting of Toronto University is the discoverer of insulin. Many hundreds, surely one is tempted to say thousands, of diabetics owe their existence to the wonderful vision and enthusiasm of this investigator. A number of men aided him in carrying out his work; it was too great a task for a single individual. C. H. Best, J. J. R. MacLeod, J. B. Collip and many others will always be associated with Banting's name in this connection.

The power of insulin to control diabetes can no longer be questioned. The reports of many able clinicians bear witness to this. It now remains for the medical profession to master the details of using this extract successfully. This is a matter that requires some study as the dosage has to be adjusted to the needs of each patient. Furthermore, if an insufficient quantity of the material is injected the diabetes is not properly controlled, whereas if too much is given there is danger of hypoglycemic shock which may be severe enough to cause death.

The preparation of insulin generally used is that distributed as "letin." This is made up in two strengths labeled U 10 and U 20, put up in 5 c.c. vials with rubber caps for hypodermic use. The U 10 label indicates that the material contains 10 units of insulin per c.c., the U 20, 20 units of insulin per c.c. The first products put out were designated as H 10 and H 20. At that time the unit was the amount of insulin which on injection subcutaneously in 2 kilogram rabbits lowered the blood sugar below .045 per cent., producing convulsions within 2 to 5 hours. Recently it has been found advisable to increase the strength of the unit 40 per cent. The stronger extract is labeled U 10 and U 20 as compared to the older and weaker H 10 and H 20.

**MODE OF ADMINISTRATION.**—Insulin must be administered by hypodermic injection. If it is given to the patient in any other way the insulin is not effective. It has been taken by mouth, by rectum, under the tongue, etc., in every conceivable manner, and in very large doses, but without resulting in control of the sugar metabolism except when the hypodermic route is resorted to. The injections should be made in a different place each time so as to avoid induration; the extract is best injected subcutaneously, not near the skin surface; intramuscular injections should be avoided. The frequency and time of injection can be taken up more intelligently after the effect of insulin on the carbohydrate metabolism has been discussed.

**EFFECT OF INSULIN ON THE BLOOD SUGAR.**—The immediate effect of insulin on the blood sugar is to lower it. This is well shown in Table 19.

TABLE 19

EFFECT OF 30 H UNITS OF ILETIN ON THE SUGAR AND CARBON DIOXIDE COMBINING POWER OF THE BLOOD

Time	Iletin	BLOOD		
		Sugar %	CO <sub>2</sub> vol. %	
8.30 A. M. ....	30 un.	.342	30.1	Fasting throughout
9.15 .....				
11.15 .....		.197	35.7	
1.15 P.M. ....		.180	38.5	
3.15 .....		.131	40.4	
5.15 .....		.104	44.0	
12.30 A.M. ....		.255	36.6	

In Table 19, one H unit of iletin lowers the blood sugar about 8 mg. This we have found to be the average effect on the blood sugar in an adult of one H unit of iletin. There are many variations in regard to this quantitative estimate and they have to be guarded against; however, there must be some guide which enables us to act rapidly especially in emergencies and this serves as one.

The time required to obtain the maximum effect of the iletin on the blood sugar in Table 19 is 8 hours; this is a little longer than the average. Table 20 in this respect more nearly represents our average result; in this patient the greatest lowering of the blood sugar occurred in 4 hours after the administration of iletin, each unit of iletin lowered the blood sugar about 7 mg.

TABLE 20

EFFECT OF ILETIN ON THE BLOOD SUGAR AND ACIDOSIS IN DIABETES MELLITUS

Time	Iletin	BLOOD			Time	URINE	
		Sugar %	CO <sub>2</sub> Comb. Power	Aceton Bodies, mg.		Sugar, gm.	Aceton Bodies, gm.
9.00...	23 un.	.308	46	33	7.48	5.7	1.25
10.00...					8.48	1.1	0.27
11.05...		.256	52	32	10.30	2.5	0.44
12.05...		.220	58	13	11.30	0.6	0.10
1.06...		.180	61	3	12.28	0.1	0.02
2.12...		.150	60	14	1.30	0.0	0.03
3.05...		.172	60	14	2.30	0.0	0.02
4.03...		.190	58	15	3.30	0.0	0.03
5.03...		.181	55	17	4.30	0.0	0.04
					5.28	0.0	0.04

*Summary.*—The usual effect of iletin is to reduce the blood sugar about 8mg. per H unit of iletin. (This applies to the H unit, the later U unit being 40 per cent stronger in its action). The maximal effect of the iletin on the blood sugar usually occurs in 4 hours after which the blood sugar rises. These are average results and great variation must be expected in individual cases.

Dr. Walters of the Eli Lilly and Company research laboratories expressed his curiosity concerning the part played by starvation in the diminution of blood sugar obtained with iletin. Accordingly we carried out the experiments shown in Tables 21 and 22.

TABLE 21

SPONTANEOUS CHANGES IN THE BLOOD SUGAR AND PLASMA CO<sub>2</sub> WHICH OCCURRED IN DIABETIC PATIENTS IN AN EIGHT-HOUR PERIOD

These patients received water only, no food was taken and no medication administered for 15 hours before and during the observation.

Time	Blood		Blood		Blood		Blood	
	Sugar %	CO <sub>2</sub> Comb. Power	Sugar %	CO <sub>2</sub> Comb. Power	Sugar %	CO <sub>2</sub> Comb. Power	Sugar %	CO <sub>2</sub> Comb. Power
9 A.M. ....	.220	50	.315	61	.280	25	.133	53
1 P.M. ....	.220	49	.272	66	.236	32	.104	47
5 P.M. ....	.140	62	.263	63	.234	35	.098	45
Change in 8 hours....	-.80	+12	-.52	+2	-.46	+10	-.35	-8

TABLE 22

EFFECTS OF ILETIN IN THE SAME CASES

The spontaneous changes are less marked in the blood sugar and plasma CO<sub>2</sub> than those after Iletin. The transient action of the Iletin should be noted.

Time	CASE I			CASE II			CASE III		
	Blood		Iletin Units	Blood		Iletin Units	Blood		Iletin Units
	Sugar, %	CO <sub>2</sub> Comb. Power		Sugar, %	CO <sub>2</sub> Comb. Power		Sugar, %	CO <sub>2</sub> Comb. Power	
8.15 .....	.200	33	5	.319	58	20	.200	44	15
11.40 .....									
1.40 .....	.110	54		.250	69		.192	58	
3.40 .....	.086	47		.197	70		.166	56	
5.40 .....	.091	46		.208	65		.187	56	
7.40 .....	.101	46		.220	64		.192	49	
9.40 .....	.119	45		.238	64		.195	48	
Change with Iletin .....	-.114	+21		-.122	+12		-.94	+14	
Spontaneous change.....	-.80	+12		-.52	+2		-.46	+10	

It is very evident from Tables 21 and 22 that insulin causes a disappearance of sugar from the blood, since the effect of insulin plus starvation is always more marked in lowering the blood sugar than starvation without insulin.

These charts serve to remind us of the fact that starvation, and other forms of dietetic treatment are not to be forgotten in the control of the blood sugar and glycosuria in diabetes. There is a fundamental difference between the control of the diabetic metabolism by diet and by insulin which must be borne in mind if these methods of therapy are to be successfully combined. While restriction of diet adjusts the food elements so that the diabetic may digest them successfully with the diminished pancreatic function at his command, insulin, on the other hand, replaces the deficient pancreatic activity and enables the diabetic to utilize an increased amount of sugar. It becomes clear that every case of diabetes does not require insulin and that when the situation does demand the use of insulin the quantity of insulin injected must be carefully adjusted to the needs of the individual patient.

**EFFECT OF INSULIN ON THE CARBOHYDRATE METABOLISM.**—It has been noted how the injection of insulin lowers the blood sugar and consequently must control the glycosuria for we know that when the blood sugar falls below .180 per cent. usually the sugar disappears from the urine. The insulin lowers the blood sugar by two means: first it brings about an increased oxidation of glucose (calorimetric

observations have shown this to be true) and secondly it results in a synthesis of glucose molecules to form the starchy substance glycogen and brings about glycogen deposition and storage in the liver and possibly in other tissues. Normally glycogen is held in reserve in considerable amounts especially in the liver and muscles. Its exact importance is unknown; that it acts as a reserve supply of glucose for the body is self evident; when the power to form glycogen is present in the body it is probable that much more effective sugar metabolism is brought about. This factor should be considered very seriously as an argument for the use of at least small doses of insulin in cases which could possibly manage to do without it. We are as yet unacquainted with the causes of the numerous complications diabetics are subject to, even though their urine be sugar free and their blood sugar normal; it may be that a deficient storage of glycogen is in part, at least, responsible for this, and that consequently a small daily dose of insulin is indicated in many patients to correct this abnormality.

A secondary effect of the increased utilization of glucose through insulin is the control of acidosis. This is taken up in the next section.

*Control of Acidosis by Insulin.*—It is a fact, recognized long ago, that the fats are changed completely to carbon dioxide and water when starches are oxidized at the same time. The statement that "the fats burn in the fire of the carbohydrates" is as true today as when it was formulated.

Since insulin brings about an increase in glucose utilization it follows that there should be a more favorable oxidation of the fatty acids and a diminution in the acidosis. Turning back to Table 20, it has already been noted that there is every indication in the blood and urine that the glucose is being oxidized in increased amounts after the injection of insulin, at the same time the carbon dioxide combining power of the blood increases pointing to a diminution of the acidosis. The same findings may be found in Tables 19 and 22. This indirect control of the diabetic acidosis by insulin is one of the most valuable effects of this extract. It furnishes the only real means we have at hand of controlling the much and justly dreaded diabetic coma.

Table 20 shows that insulin improves the diabetic acidosis not only as measured by an increase of the carbon dioxide in the blood, but also by a control of the acid substances, directly; thus the acetone bodies in the urine rapidly diminish to the vanishing point (there are traces of these materials even in the normal urine) and the same is true in the blood. This completes the chain of evidence that insulin does cause an increased consumption of glucose in the diabetic and in doing so brings about a better oxidation of the fatty acids, thus combating both glycosuria (and hyperglycemia) and acidosis.

*Hypoglycemic or Insulin Shock.*—The one great danger in the administration of insulin is the lowering of the blood sugar below the normal level. It is generally conceded that when a hypoglycemia of .045 per cent. or 45 mg. of blood sugar per 100 c.c. is reached, that certain symptoms follow which may terminate fatally. These symptoms are: marked hunger, nervousness, pallor, sweating; the patient appears and acts like a person who is about to faint; a more or less violent delirium may come on, or there may be marked vertigo and weakness to be followed by convulsions, collapse, unconsciousness and death.

The blood sugar level at which hypoglycemic shock appears is not constant. It varies as do all the effects of insulin markedly in different individuals. Thus Table 23 gives the data in a case which exhibited hypoglycemic symptoms while the blood sugar was at a low normal level only.

TABLE 23

MODERATE "hypoglycemic shock" WITH BLOOD SUGAR OF .075 PER CENT.  
FEMALE—*Diabetes Mellitus*.

Time	Insulin	Blood		
		Sugar, %	CO <sub>2</sub> Comb. Power	
9.00 .....	10 un.	.183	58.6	Fasting throughout.
9.00 .....		.075	59.5*	
11.00 .....		.083	53.8†	
1.00 .....		.111	52.8‡	

This may be contrasted with Table 24 in which there was no ill effect even though the blood sugar dropped to .052 per cent.

TABLE 24

No signs of "hypoglycemic shock"; in spite of blood sugar at level of .052 per cent.; seems brighter than in several days.

BOY—*Diabetes Mellitus*. Age 12.

Time	Insulin Units	Blood		
		Sugar, %	CO <sub>2</sub> Comb. Power	
8.30 A.M. ....	15	.326	38.5	Fasting throughout
9.30 A.M. ....		.052	47.5	
12.30 P.M. ....		.064	39.5	
3.00 P.M. ....				

There are cases on record in which the blood sugar has dropped lower than this without producing any symptoms whatsoever, but it is not a safe chance to take.

The treatment for hypoglycemic shock is to give the patient some readily absorbed form of carbohydrate as soon as possible; orange juice and about one ounce of sugar (1 heaping tablespoonful), preferably glucose, to be repeated at 15 minute intervals if necessary. In unconscious or marked cases, a glucose infusion of 10 to 50 per cent. strength should be used if possible, otherwise a glucose or sugar solution may be given by stomach tube.

The rapidity with which the blood sugar is lowered may have some bearing on the production of hypoglycemic shock. A very rapid diminution of the glycemia may result in symptoms whereas a more conservative handling of the situation will not do so. Hence, especially in the treatment of coma patients, repeated injections of insulin are preferable to a single large one.

*The Frequency and Size of Insulin Dosage.*—Insulin is usually administered just before meals. The object is to have the insulin act upon the hyperglycemia following each meal and also to prevent a hypoglycemic reaction which might occur if the insulin administration were not followed by food.

\* 11.00 weakness, pallor, perspiration, tremor hands.

† 1.00 same symptoms but less marked.

‡ 3.00 comfortable but still weak.

The number of doses of insulin per day may be one, two or three. A single large dose may be given, usually before breakfast, but in any event immediately preceding the meal containing the greater portion of the protein and carbohydrate of the day's food.

When the food is evenly, or fairly evenly, distributed throughout the day two or three injections may be used. This is the procedure that is carried out in most cases at the present time. From what has been previously said it is probable that the effect of any one insulin treatment is terminated in about 8 hours, it is therefore advisable, if the blood sugar is to be controlled throughout the twenty-four hours, to give at least 2 injections.

TABLE 25

## DIET—SAME ON EACH DAY

*Effect of one, two, or three doses of Insulin a day on the blood sugar (B. S.).*  
 MALE—Diabetes Mellitus.

Time	Insulin	B.S.	Insulin	B.S.	Insulin	B.S.
7 A.M.....	30 un.		15 un.		10 un.	
7.30.....	Breakfast					
10.....		.266		.272		.284
11.45.....	0		0		10 un.	
12.15.....	Lunch					
3.00.....		.272		.274		.312
4.45.....	0		15 un.		10 un.	
5.15.....	Supper					
7 P.M.....		.312		.274		.284

In Table 25 it is shown how the blood sugar rises during the day when a single dose of insulin is administered, whereas it remains fairly constant either with two or three administrations. Since the comfort of the patients demands as few injections as possible, two in this patient, as in most, would be the choice.

It must be remembered that to obtain the best results the frequency of insulin dosage may have to be varied in individual cases for many reasons. No iron-clad procedure in this respect should be followed by any physician or institution.

The size of the dose of insulin requires a great deal of experimentation for proper adjustment to the patient's needs.

In the first place a small dose (one to five units) should be given on two or three occasions to determine whether the material produces toxic effects or whether the patient is particularly susceptible to hypoglycemic shock. If neither of these conditions exists—1 unit of insulin may be ordered per day for every 3 or 4 grams of glucose present in the 24 hour urine; or one unit may be given for every 12 milligrams it is desired to reduce the blood sugar during the day. (This of course supposes that the patient is being kept upon a diet constant in weight and in the proportion of fat, protein and carbohydrate.) Subsequently the insulin is increased or diminished as the glucose of the blood and urine indicate; the ultimate object is to have the urine sugar-free, the blood sugar at a normal level and enough food value to furnish maintenance without undue gain in weight.

The actual amount of starch accounted for by one unit of insulin varies a great deal in different patients. There are occasional cases in which little or no sugar at all is digested; this is particularly true in older individuals with arteriosclerosis and in the presence of complications, especially infections. The average amount of sugar apparently

utilized by the unit of insulin is shown in the experiences had with one case given in Table 26.

TABLE 26

MALE—*Severe Diabetes Mellitus.*

(Gms. glucose utilized per H unit ofletin.)

Apr. 10.....	1.9 gms.	Jul. 11.....	2.0 gms.
20.....	2.6 "	16.....	2.0 "
May 7.....	2.3 "	25.....	1.3 "
15.....	0.6 "	Aug. 3.....	1.6 "
25.....	1.8 "	Sep. 7.....	1.4 "
Jun. 5.....	1.6 "	17.....	1.4 "
18.....	2.2 "	26.....	1.9 "
29.....	1.7 "	Oct. 1.....	2.0 "
Jul. 6.....	1.8 "	18.....	1.8 "

Another point to be remembered in gauging the proper dosage of insulin is that small injections often have a very much greater effect per unit, than larger doses; thus the use of 10 units may digest 3 grams of glucose per unit, 20, two per unit, while 40 may only bring about the utilization of 1.5 grams of glucose per unit. It is evident that there are many advantages in small doses besides economy; by diet adjustment the insulin dosage may often be regulated indirectly.

The use of insulin in diabetic coma is taken up in the section on the treatment of coma.

THE TREATMENT OF COMPLICATIONS OF DIABETES MELLITUS.—It would lead us too far afield to take all of these up in detail. The tendency on the one hand has been to exaggerate their importance. Any complications of diabetes, infections, gangrene, appendicitis, carbuncles, etc., should be handled as though the diabetes did not exist with the possible exception that if it is at all feasible time should be allowed the physician to attempt to set aside glycosuria, acidosis and arrive at a maintenance diet before the surgeon steps in; in emergencies of course the medical and surgical procedures may have to be resorted to simultaneously. It is remarkable what satisfactory results may be achieved, and how little there is to fear in many instances when the diabetes is properly controlled. On the other hand there is a group of medical men who from a limited and fortunate experience believe that surgery may be resorted to in diabetes without regarding the dietetic or insulin control of the situation. This is a reprehensible procedure and will entail disastrous consequences sooner or later.

There is no condition whose mortality has been more efficiently checked than diabetic coma as controlled by insulin. Whereas formerly the patient who was drowsy with diabetic acidosis was almost certain to succumb in 48 hours we find now that he is almost as sure to live instead of dying. Change from a bad to a good prognosis has been brought about by the use of insulin.

There are many points that have to be looked after and adjusted in the treatment of diabetic coma; these are:

1. Coma in diabetes is preventable if the diet has been properly supervised. A proper relation of the fatty acids to glucose in the diet as previously discussed, is the almost invariably successful prophylactic therapy for diabetic acidosis.

2. Rest in bed.

3. Warm blankets, hot water bottles, a warm well ventilated room.



4. Cardiac stimulants—preferably digitalis—the heart is often extremely weak and may exhibit marked tachycardia.

5. Forcing fluids—by mouth—at least three quarts a day; if the patient is very much desiccated, as is often the case, hypodermoclyses or retention enemata may be resorted to at the outset.

6. The bowels should only be moved after the patient has retained some fluid; constipation is often the result of excessive dryness of the intestinal contents; enemata are the most suitable means.

7. Allow sodium chloride in good amount with the food and salty liquids, as broth; it serves to favor the retention of fluid in the tissues.

8. Bicarbonate of soda three to five grams in a full glass of water every hour or two aids in the elimination of the retained acid substances and diminishes them in the circulation; it also effects a retention of fluid in the tissues. In unconscious patients the bicarbonate of soda may be given as a 5 per cent. solution by infusion. The use of this drug should be controlled by frequent observations of the blood  $\text{CO}_2$  so as to be certain that an alkalosis is not produced.

9. *Diet.*—Fats must be avoided absolutely. Proteins may be given in small amounts. Starches in moderate quantities. Such diets are detailed as "Acidosis Diet," page 122. It is useless to force starches in most cases, as the body is already surfeited with glucose and the problem is rather to bring about an oxidation of the material present than to overload the staggering pancreatic function with a still greater burden.

The use of insulin in diabetic coma demands much good judgment, courage to act quickly or to wait, and much hard labor to obtain frequent laboratory determinations. A proper routine of insulin dosage in severe diabetic acidosis and resulting coma or threatened coma would be somewhat as follows:

1. An initial dosage of 40 units of insulin (20 units subcutaneously and 20 units intravenously).

2. Ten to twenty units of insulin hypodermatically every four hours. (The facts upon which these procedures are based have been discussed but may be repeated:

(a) Small doses of insulin frequently repeated are more effective than single large doses.

(b) The maximal result of each dose of insulin usually occurs at the end of four hours.

(c) If the blood sugar is lowered too rapidly insulin shock may occur, even though the level of the blood sugar is still high.)

3. When the urine becomes free from sugar, the combining power of the blood for  $\text{CO}_2$  reaches 40, the blood sugar reaches a level of .200 per cent. and the patient's condition is improved, the whole treatment may be changed to that detailed under the treatment of diabetes mellitus. This usually requires several days.

4. The blood sugar and  $\text{CO}_2$  combining power of the blood should be determined frequently, at 4 or 6 hour intervals. If the blood sugar approaches normal and the  $\text{CO}_2$  values remain low, as is usual with obstinate cases, an infusion—200 c.c. of 10 or 20 per cent. glucose—may be given. At the same time 1 unit of insulin for about every four grams of glucose administered is injected intravenously.

5. Variations from the above will naturally suggest themselves as each case is studied. It is impossible to plan the campaign for each

patient more than a few hours in advance. When the more intricate laboratory procedures are not at hand the general condition, the depth of the respirations and frequently repeated urine analysis will serve as adequate guides for the dosage of insulin.

**BLOOD SUGAR AS A GUIDE TO TREATMENT.**—It is frequently possible from blood-sugar determinations to predict when glycosuria is about to manifest itself. It has been mentioned that the normal renal threshold to glucose is approximately 0.17 per cent. With a rising blood sugar, the increase in the food should be stopped when the glycemia reaches a level of about 0.15 per cent. Taking advantage of such findings will often shorten the period of observation necessary to determine carbohydrate tolerance by a considerable margin.

The object of many physicians has been to attempt to maintain the blood sugar of all diabetics at a normal level. This would seem to be the ideal condition; however, it cannot be obtained in every instance. There are many patients whose hyperglycemia, though it may be 0.2 per cent. and even higher, show no sugar in their urine, and, from a clinical point of view, run a very favorable course. What effect such a constant hyperglycemia will have on the body and its functions remains an open question. Whether arteriosclerosis, gangrene, nephritis, cataract, infections, etc., are more prone to develop under these circumstances, is not finally determined. Mosenthal, Clausen and Hiller have recently shown that diabetics with a higher level of blood sugar apparently utilize ingested carbohydrate to better advantage than those with a normal glycemia. It may be, therefore, that it will not be to the greatest advantage to reduce the blood sugar to normal in every case of diabetes mellitus.

**Course and Prognosis.**—The *clinical course* and consequently the *prognosis* of the disease is extremely varied. There have been rare instances in which patients once afflicted with this malady were reported as completely cured. The writer has seen only one case that approached this desirable result. This was an obese woman who was operated on for umbilical hernia and subsequently had a moderately severe type of the disease. In the course of six months she gradually recovered her carbohydrate tolerance so that she was again able to eat without restriction. For three years the condition showed no change. Recently she has been heard from, 6 years after her operation and marked glycosuria, and she says that she again has large amounts of sugar in her urine. Such experiences certainly generate much skepticism in regard to the possibility of a permanent cure in diabetes.

As a rule, the disease has a tendency to progress, and carbohydrate tolerance to diminish. There are many individuals who form an exception to this rule. It has seemed to the writer that the exception was most frequent in elderly, rather obese, individuals. Age has always been regarded as an important prognostic factor. Von Noorden formulated the average duration of life in this disease as follows:

<i>Age (Years)</i>	<i>Duration Life (Years)</i>
1-10	2
10-20	4
20-30	6
30-40	10-15
40 +	Very mild.

Riesman has called attention to a very mild type of diabetes, occurring in adolescence and childhood; the general features of this are a familial tendency, a very low-grade glycosuria, and a normal blood sugar. In other words, these cases present the general features of renal diabetes or glycosuria. Whether they actually fall in this category remains to be determined. On the other hand, there are some cases whose progress is much more rapid than von Noorden indicates. The writer has met with a considerable number of patients of between 35 and 45, in whom the disease advanced with extreme rapidity. It is well not to lay too much stress on our knowledge concerning the course of diabetes, and give a very guarded prognosis. Mention has already been made that Joslin believes that the hereditary cases have a tendency to be mild.

In former year, the diabetes of the more progressive type terminated in coma. To-day, as the result of more scientific management of the diet, this is not so common, and inanition may be considered as playing more of a rôle. In those patients in whom the disease does not advance rapidly, it is found that hypertension, arteriosclerosis and its complications, nephritis, cerebral hemorrhage, gangrene of the extremities, etc., are prone to close the picture. Especially in neglected cases of this type, the infections—septicemia, furunculosis, tuberculosis, etc.—may develop as terminal events.

Thus far, for a period of more than a year, Insulin has been effective in prolonging the lives of diabetics who are faithful and conscientious in carrying out the prescribed treatment. There is no reason to suppose that this cannot be accomplished indefinitely.

## CHAPTER VII

### DIABETES INSIPIDUS

BY WILLIAM FLETCHER MCPHEDRAN, B.A., M.B.

Definition, p. 135—Etiology, p. 135—Predisposing causes, p. 135—Symptomatology, p. 138—Clinical history, p. 138—Physical examination, p. 139—Laboratory findings, p. 139—Special examinations, p. 139—Functional tests, p. 139—X-ray examinations, p. 140—Diagnosis, p. 140—Complications and association with other diseases, p. 140—Clinical varieties, p. 140—Treatment, p. 140—Prophylaxis, p. 140—Medicinal treatment, p. 141—Surgical indications, p. 142—Prognosis, p. 142—Pathology, p. 142—References, p. 143.

**Definition.**—This disease is characterized by the elimination of a large quantity of urine of lowest specific gravity, low in salt and nitrogen content, by thirst, and frequently by evidences of involvement of the pituitary gland.

**Etiology.**—**PREDISPOSING CAUSES.**—*Sex.*—Males are more likely to be affected with diabetes insipidus than females.

*Age.*—The majority are all young persons. Strauss (quoted by Fletcher) found nine cases under five years of age, and fifty-seven out of eighty-five under twenty-five years of age.

*Heredity.*—Heredity is thought to be a prominent influence. Weil has quoted twenty-three out of ninety-one persons in four generations who had persistent polyuria, without any deterioration of health. These cases were congenital and persisted throughout life.

*Effects of Exposure—Excessive Drinking of Water.*—Patients have occasionally dated their illness to these causes.

*Mental Shock.*—This is also supposed to have given rise to the disease.

*Trauma.*—A good many cases have been reported following injuries to the brain. Fractures and bullet wounds, particularly when the projectile remains in the skull, have set up the disease in several instances.

*Syphilis.*—The importance of syphilis in causing irritation, either by the gumma or meningitis, in the basal region, must not be overlooked. It is easily understood how these inflammatory changes might cause the polyuria, when one remembers the ease with which polyuria is produced experimentally, by lesions to the cerebellum or to the pons.

*Failure of Renal Activity.*—Since Magnus and Schaefer first showed the connection between the pituitary body and renal activity (1901), there have been many papers dealing with the influence of this gland on the various aspects of kidney activity.

The pituitary gland weighs about 0.5 gram, and is situated at the base of the brain, lying in the sella turcica (*see* Fig. 1). It can easily be split in two parts, the anterior or *pars glandularis*, and the posterior or *pars nervosa*. The cleft separating the two represents the remains of the original tubular structure, from which the anterior part was developed from the epithelium of the mouth cavity. The anterior part, or *pars glandularis*, is more vascular, and from it Robertson<sup>1</sup> has procured his substance, tethelin, to which he attributes the governing of growth. The posterior part is composed of nerve cells and neuroglia, and contains a great deal of hyaline material that is believed to be the substance secreted by the gland. It is the extract that is used in medicinal practice.

The blood-supply is small, that is to say, the granular material

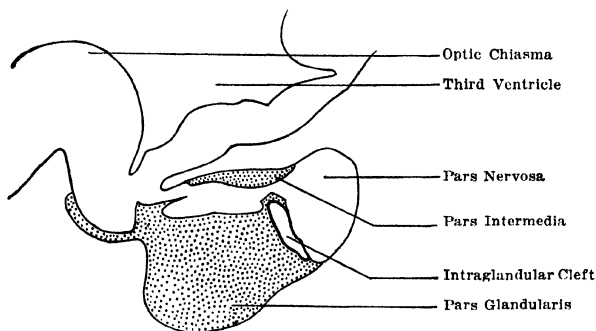


FIG. 1.—DIAGRAM OF PITUITARY GLAND.

forming the extract is much more slowly put into the circulation than is that of the anterior lobe.

Between the posterior lobe and the cleft separating the two lobes is a layer of cells known as the *pars intermedia*. It is believed by some writers that the *pars intermedia* gives off a material quite similar to that found between the cells of the posterior lobe.

The removal of the posterior lobe can be withstood to a striking degree. The extracts from the lobes not only act directly on the involuntary muscle fibers, but increase the activity of the mammary glands and the kidneys. This latter effect is a marked diuresis, which may be due to a dilatation of the vessels; but the high output of urine continues after the evidence of increased blood-flow in the kidney has disappeared. It is believed by some authorities that the action is that of a definite secretory hormone and that it is independent of the vascular changes.

All of the experiments carried out on increased renal activity and increased blood-pressure have been performed on animals. In man, the results obtained have been very contradictory. Several observers

have found increased amounts of urine output following subcutaneous injections of pituitrin, whereas Van der Velden was able to stop diuresis in two normal men by injecting hypophysis extract; and later in the same year Frey and Kumpiss repeated this experiment with the same extract. Motzfeldt<sup>2</sup> found, in 1914, that the injections of pituitrin extract checked diuresis in fifteen apparently healthy patients. Since then there have been many papers dealing with the relationship of pituitary extracts to diuresis, whether that of diabetes insipidus or of an artificially induced polyuria. Motzfeldt in one case found that feeding the posterior lobe checked the diuresis, while the anterior lobe had no such effect. In the second patient, four pituitary lobes taken at night proved sufficient to check the diuresis so much that she was able to enjoy a good night's rest. In the third instance, the amount of urine passed diminished from 6,000 c.c. to 1,500 c.c. on the subcutaneous administration of pituitary extract. He found later that when polyuria had been developed by water-drinking in animals, the extract of the posterior lobe of *pars intermedia* given by mouth subcutaneously or intravenously, was able to stop this polyuria. He found this effect was constant, and that it was independent of the changes in blood-pressure, intestinal absorption, or the vagi. It was apparently prevented or delayed by division of the splanchnic nerves, and was likewise reduced by division of the renal nerves. Hence, he thought that the antidiuretic effect was obtained by stimulation of the sympathetic nervous system and that the renal vasomotor system was of the greatest importance. On this basis he argued that the polyuria of nervous disorders was organic or functional, and those due to pituitary gland disturbances were very closely associated.

No effect on the polyuria was obtained by most drugs or by other gland extracts, except caffeine in large doses and adrenal cortex extracts. Christie and Stewart<sup>3</sup> showed, in a similar case, that when the extract was being administered to a patient suffering from diabetes insipidus, the blood-flow in the arm was increased. This was of some importance, in support of the view that a vascular effect in the opposite direction—that is to say, a dilatation of vessels other than those in the kidney—may be responsible for the diminution of the output when pituitary extract is administered. Under the action of this extract the patient was able to concentrate the urine to a considerable degree; but without the extract the total excretion of salt and nitrogen was quite normal. Claussen<sup>4</sup> found that the administration of the extract checked the water and chlorid flow invariably, but the output of urea was not affected at all. When the hourly ingestion of water and sodium chlorid is maintained at a high level, there is little influence on the urea elimination by pituitary injection, whereas the chlorid elimination is considerably reduced, and the water elimination very greatly reduced.

Addis, Barnett and Shevsky<sup>5</sup> found no conclusive evidence that pituitary extract alters the activity of the kidney. They found that when the diuresis was not brought about by the ingestion of water, the volume of urine passed might be increased by intravenous administra-

tion, or decreased by subcutaneous administration. The kidney secretion of water might, they thought, be influenced by the pituitary extract, or the amount of water available might be altered. They also showed that the subcutaneous administration of the extract was followed by a marked depreciation of the urea-excreting activity of the kidney. If an increased amount of urea was available for excretion, the degree of change produced by pituitary extract was less than when the urea available for excretion was low in amount. That is to say, they did not believe the extract had much effect upon the excretion of urea.

Barker and Mosenthal<sup>6</sup> have made an interesting study of a patient with an excretion of over eight liters, who had relief from the extract. When the extract was given, the amount was reduced to two and one-half liters. The amount of sodium chlorid was not appreciably changed, but its concentration could be raised greatly under the influence of the pituitrin. The same was true of nitrogen. They experienced no good effects from the extract used in any other way than by injection.

Eric Meyer<sup>7</sup> has been the leading exponent of the failure of kidney activity as a cause of diabetes insipidus. He felt that it was due to a primary polyuria, because the kidney was unable to secrete normal concentrated urine; that is to say, the patient had to take large quantities of water to excrete the salts and nitrogenous end-products, whose retention would result fatally. However, recent studies on functional tests, and the action of pituitary extract, show fairly definitely that the disease cannot be explained by this hypothesis.

None of these experiments, however, throw any light on the congenital cases. They remain the mystery that they have always been.

**Symptomatology.**—CLINICAL HISTORY.—*Mode of Onset.*—Diabetes insipidus may begin suddenly, with a tremendous thirst. Occasionally it may be preceded for a year or two by a feeling of lassitude and listlessness. They usually have to rise very frequently at night to empty the bladder; simultaneously they notice that they are drinking large amounts of water at one time.

*Symptoms during Progress of Disease.*—Thirst is a predominant symptom. Patients frequently drink a whole pitcher of water at once. One of Trousseau's patients drank fifty liters in twenty-four hours. The lengths to which patients deprived of water will go to procure fluid for intake are remarkable. They will stop at nothing. Newmark<sup>8</sup> tells of a patient of his who, associated with thirst for water, had an inordinate appetite for alcohol, and drilled holes into wine barrels to suck up the contents through a straw, thus emptying the barrels in a very short time.

Other symptoms are rarely observed. There may be palpitation of the heart, and various digestive disturbances, such as discomfort in the abdomen, and eructation of gas. The appetite varies considerably. In some instances it is undisturbed, but in others it may be ravenous. One of Trousseau's patients ate at a Paris restaurant where the meals were served at a fixed price, with bread included. He ate so much

lead that the restaurant proprietor found it to his advantage to pay him to keep away. Sweating may be absent. In spite of the large amount of fluid imbibed, constipation may be a distressing factor.

In cases that are accompanied by tumors of the infundibular region, there may be severe headache, bitemporal, hemianopsia, and inflammation or degeneration of the optic disk. The individual's weight may undergo no change, but occasionally there may be a great decrease.

**PHYSICAL EXAMINATION.**—Rarely is there any marked abnormality to be found. The skin is generally clear, soft, and rather dry. In spite of the fact that one frequently finds abnormalities in the posterior lobe of the pituitary gland, the bodily hair is usually normal in amount and distribution. The patient may be stout. There is rarely any edema (except in the terminal stages). Quite frequently the blood-pressure is raised, and shows a tendency to vary. Whereas in diabetes mellitus, the reflexes are apt to be diminished; in diabetes insipidus they frequently are exaggerated.

**LABORATORY FINDINGS.**—*Blood.*—The blood is quite frequently raised in content of red blood-cells and hemoglobin. This is remarkable, in view of the large amount of fluid that must be passed through it.

*Urine.*—The increase in the amount voided is a characteristic symptom of the disease. Trousseau had a patient who passed 43 liters in a day, and Vierordt a child who passed 12.3 kilograms, the child weighing 13.2 kilograms (29.1 lbs.). The usual amount voided ranges between 7 and 15 liters. This is passed in amounts of from 175 to 560 c.c. per hour. The specific gravity is from 1.001 to 1.005. Occasionally, evidences of albumin or leukocytes are found. The color is pale, with possibly a bluish tinge. The amount of chlorid passed in the day depends upon the amount taken in, and the same is true of the nitrogen in its various partitions.

The various kidney functional tests have been done, notably by Barker and Mosenthal.<sup>6</sup> These tend to show that the amount of solids excreted is fairly constant on a reduced urine output as well as when the individual has had an adequate amount of water to drink.

**SPECIAL EXAMINATIONS.**—*Functional Tests.*—Kidney functional tests have been performed by numerous observers, notably Mosenthal, and the functions have usually been found normal.

It has long been known that diabetes insipidus is often the accompaniment to disturbances of the brain. Fletcher<sup>9</sup> has noted the incidence of cerebral syphilis as a cause of the disease; in four patients it seemed likely, because of the history, symptoms, and improvement under potassium iodid, that luetic infection was the cause. As in many other diseases, a Wassermann reaction should be performed, and in diabetes insipidus it should be carried out also upon the cerebral spinal fluid.

Independent of the use that will be made of pituitary extract as a therapeutic measure, its employment for diagnosis cannot be too highly recommended. The degree to which the concentration of sodium chlorid and of nitrogen may be raised, and the reduction in the amount and



increase of specific gravity are remarkable in almost all the cases reported in the last six years. This change produces a striking improvement in the patient's feeling of wellbeing.

**X-ray Examinations.**—An examination by x-ray is of great importance, because many cases follow injury to the skull by fracture of foreign body. There have been several cases reported, of the finding of polyuria, following the lodging of a bullet in the cranial fossa. While in a good many instances the sella turcica may be found enlarged, there are others in which the history, examination, and therapeutic test of the pituitary gland extract leaves little doubt in the physician's mind that the disease is due to pituitary involvement, and yet the gland area on examination with the x-ray is quite normal.

**Diagnosis.**—The diagnosis is simple. It is made on the large amount of urine passed per day, persistent for a long time. Increases in the amount of urine voided are also found in *chronic interstitial nephritis*, but in the latter, if the amount is raised greatly, the presence of albumin and a few casts, the evidences of affection of the heart and great vessels, together with the performance of various kidney functional tests, should make the diagnosis simple.

Polyuria is also a common accompaniment to *hysteria and various other cyclical disorders*. Here it is apt to be intermittent in character, and the mental state differs greatly from that of the sufferer from diabetes insipidus. However, when one experiences polyuria extending over a lengthy period, one must be careful not to ascribe it to purely neurotic influences. Newmark's case (*see* section on Pathology) is interesting in this regard. Here the individual had no clinical signs of a brain tumor, except the polyuria, for many years; then, the classical signs of headache, vomiting, and optic neuritis were evident for two weeks before death.

**Complications and Association with Other Diseases.**—There are rarely any complications of diabetes insipidus, nor is it commonly found associated with other diseases.

**Clinical Varieties.**—It is customary to divide the disease into two groups: (1) the primary or idiopathic group, including the hereditary cases with a constitutional defect either in the kidneys or, possibly, in the pituitary gland; and (2) the symptomatic group, comprising cases which give a definite history of either disease of the pituitary gland or lesion in the brain that, by pressure, has destroyed the function of the pituitary gland. Included among the latter are the traumatic, the infective—such as tubercular or syphilitic—and the metastatic cases. In the latter are included those who have had a malignant disease and have later developed polyuria. In many patients with cancer, who have had polyuria, metastases in the region of the pituitary gland has been found at autopsy.

**Treatment.**—**PROPHYLAXIS.**—There is no prophylactic treatment of diabetes insipidus. In families where there is a history of the disease, it would be well for the individuals to **keep a record** upon the development of inordinate appetites, thirst, or polyuria.

Cases have frequently been reported since 1913, that have been influenced by the therapeutic use of **pituitary gland extracts**. Enough cases have been reported which have been treated by this means, for one to be sure that the effects are satisfactory and unlikely to produce any ill effects. If the disease of the pituitary gland is organic, treatment will be required for a long time—perhaps for the term of the individual's life. It is customary to give about two or three injections, of 1 c.c., in the twenty-four hours. The effect lasts only, at longest, seven to eight hours. When enough is given to contro. the symptoms, the amount of urine voided will be practically normal. The injection is best given intramuscularly or subcutaneously. Any standard preparation of pituitary gland may be used. The most favorable effect is obtained with two or more injections, of not less than 1 c.c. each, and given in the twenty-four hours. It is usually observed that the reduction after the second dose is more noticeable than after the first. The urine is reduced greatly in amount, and raised in its salt and nitrogen concentration. For example, the individual may pass 300 c.c. per hour while not under the influence of pituitary gland extract; following the first injection, the volume may drop down to 180, and following the second, there will be still further reduction, down to 75 or 80 c.c. per hour, which is about normal. The effect, however, does not last very long. If its influence is lost, the amount of urine passed rises rapidly, and the concentration of sodium chlorid and nitrogen are again reduced.

Long-continued use of the pituitary gland extract does not seem to result in a loss of its effect. Neither the interval nor the amount of substance used should be reduced. While Motzfeldt<sup>2</sup> has reported a successful treatment of the disease by feeding the fresh glands, the majority of case reports have shown that intramuscular, subcutaneous or intravenous administration of the aqueous extract have been the only successful methods of administration. In Motzfeldt's experiments on rabbits, he checked the diuresis after gland substance administration, but the amounts used were very large. Sometimes, fifty times the dose that was sufficient on subcutaneous administration was necessary.

Extracts of other glands of internal secretion have been tried frequently, but in no case has any effect ever been noted, produced by adrenal or thyroid extracts.

**MEDICINAL TREATMENT.**—The medicinal treatment is most unsatisfactory. Futcher says the long list of drugs recommended is ample evidence of their general inefficiency. **Opium** and **codeia** have been given at times, in the usual doses, without any effect except, possibly, to lessen the intense thirst. **Valerian** 0.3 gram (4.6 grains) of the powdered root, increasing to 8 grams (2 drams), was the most commonly used drug. **Ergot** in the fluid extract has also been advised.

If there is any history of luetic infection or, on careful examination, any manifestation of the disease is present, or if the Wassermann reaction (which should most certainly be performed) is positive, energetic treatment should be employed. This, in view of involvement of the nervous system, should commence with **potassium iodid** and **mercury**,

followed later by the use of **arsenphenolamin**. The potassium iodid may be given in solution in milk, starting with five drops of the saturated solution three times a day, and increasing a drop a day until the patient has symptoms of iodid intoxication. That is to say, the patient receives five drops three times the first day; on the second day, six drops once and five drops twice; on the third day, six drops twice, and five drops once; and on the fourth day, six drops three times. More effect will probably be obtained by this gradual increase of the iodid than if the individual were suddenly saturated with the drug. The mercury may be administered as an inunction, either of the metallic mercury or of calomel.

**SURGICAL INDICATIONS.**—Occasional relief, and even complete cure, is obtained from the performance of a lumbar puncture, and Graham<sup>10</sup> has reported one such case where a man had fallen and probably fractured his skull. The amount of urine voided was about ten liters per day. There was evidence of slight inflammatory changes in the optic disks. When the lumbar puncture needle was introduced, the fluid squirted out eight or ten inches. To the intense surprise of all concerned, the amount of urine diminished greatly, and the patient's symptoms of headache, thirst and malaise disappeared completely.

Other observers have not been nearly so fortunate. Barker's patient was quite uninfluenced. It is, however, a very simple procedure, and should be done from a diagnostic standpoint at any rate, because many individuals suffering from syphilitic infections of the nervous system have a negative Wassermann reaction of the blood and a positive reaction of the cerebrospinal fluid.

**Prognosis.**—The idiopathic type has a much more favorable outlook than the symptomatic, that is to say, than the one in which definite evidence of organic disease of the nervous system can be found. Not only is the patient liable to suffer from the diabetes insipidus, even showing pronounced emaciation and weakness, but the primary disease causing a pressure or damage to the nervous system—here particularly the pituitary gland—is likely to be of serious moment.

As the time since the introduction of the free use of the pituitary is short, it is not advisable to discuss the ultimate prognosis in the case treated by this means.

**Pathology.**—Occasionally the pituitary gland will be found to be affected by various processes after death. Sekiguchi<sup>11</sup> has recently reported two cases of breast cancer metastasis in the posterior lobe of the hypophysis, in both of whom, exhibited at the end of life, there was severe polyuria. Newmark<sup>8</sup> has written of one case who died at the age of fourteen years, having had diabetes insipidus for the last five years and the cardinal signs of tumor of the brain (headache, vomiting, optic neuritis) for the terminal two weeks only. The tumor that probably caused the disease occupied the infundibulum, between the frontal lobes, and had destroyed the hypophysis. He has reviewed many of the cases reported, wherein gross lesions have been found at autopsy, and states that the tumors found generally occupy the infundibular

region and exercise their effect by pressure on the hypophysis. From the history of these patients who had severe polyuria for so long, and definite symptoms of brain tumor for so brief a time and yet, at autopsy, had a tumor which must have existed (from evidences of its slow growing character) for many months, he cautions against the advisability of considering the idiopathic class of the disease as really existent. He feels that it is probable that all cases have an organic nervous cause.

The kidneys are occasionally found enlarged and hyperemic. There is often dilatation of the ureter and the kidney pelvis. The bladder is generally dilated and its walls thickened.

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## CHAPTER VIII

### RICKETS

(*Rachitis*)

BY FRANK C. NEFF, M.D.

Definition, p. 145—Etiology, p. 145—Predisposing causes, p. 145—Diet, p. 147—Experimental studies, p. 148—Symptomatology, p. 149—Physical findings, p. 149—Laboratory findings, p. 152—X-ray findings, p. 152—Diagnosis, p. 152—Complications, p. 153—Sequelæ, p. 154—Association with other diseases, p. 154—Treatment, p. 155—Prophylaxis, p. 155—Diet, p. 156—Medicinal treatment: general management, p. 156—Prognosis, p. 157—Pathology, p. 157—Gross changes, p. 157—Minute changes, p. 158—Chemical changes, p. 158—Other changes, p. 158—Historical summary, p. 159—Sociological aspects, p. 159—References, p. 160.

**Definition.**—Rickets is the most common nutritional and metabolic disturbance in infancy, characterized by a loss of mineral salts from the bones with resulting deformity. That the nervous system is also involved is seen in the restlessness and in the tendency to convulsions. The disease is protean in its manifestations, evidenced by the many symptoms and clinical changes which will be described. So-called fetal rickets and the condition known as true late rickets are different from the ordinary rickets of infancy and will not be described in this chapter.

**Etiology.**—PREDISPOSING CAUSES.—The onset of rickets is in the winter months, due not to the cold weather *per se*, but to the various factors concerned in the housing at this time of year. In fact certain countries such as the arctics and the mountainous regions are relatively free of rickets. The disease is usually regarded as one of the temperate zones, where undoubtedly it is widely distributed. The further investigation is carried the more evidence there is that, with a few exceptions, the disease is common the world over. It has been reported frequent in northern Africa and in the West Indies. That the *climate* is not *directly responsible* will be seen from our further study of the etiology. The prevalence is thought by certain writers to be somewhat influenced by *sex*, nearly twice as many boys as girls being affected.<sup>1</sup> This conclusion has been reached in the search for rachitic sequelæ among older children. No explanation of this frequency among males has been offered. Rickets is slow in onset, and the child is usually *beyond the age of six months* before the disease is manifest. From six until twenty-four months is the time of life in which the incidence is found. This corresponds to the period of great activity on the part of the bone-forming

tissues, likewise to the time of greatest dependency and helplessness on the part of the child. There is a marked *racial tendency* to the disease among the Negroes and Italians, especially among the peoples transplanted to the cities. Heredity as regards race thus plays a part. In Negro families of our large Northern cities, nearly every child develops the disease. In England, Gilmour<sup>2</sup> found that the younger members of large families are more apt to be found with stigmata of rickets than are the older members.



FIG. 1.—DEFORMITIES IN RICKETS.

Brother and sister, aged three and five years, members of an Italian family in which there is a younger child, all three with marked rachitic deformities.

It is recognized that the disease is generally one of the *poorer classes*. There are many reasons for this, such as: the larger families and the absolute and relative greater number of offspring among the poor, the economic difficulty of giving the healthful attention needed, the increased ignorance which is so commonly an accompaniment of poverty, and the lack of suitable living quarters.

In England rickets is said to be common in the country, while in Norway there have been found nearly as many rural as urban cases. In the United States the disease is more prevalent in the cities. The greatest poverty, both as to percentage and as to degree, is in the crowded communities. This is reflected not only in the more frequent artificial

feeding, in the quality and varying degree of freshness and even in the quantity of the child's food, but in the air space of the home and the difficulty of securing pure fresh air out of doors. Bad hygiene and overcrowding is the lot of the poor.\* For the same reason institutions as homes for infants are often wholesale offenders. Most physicians are familiar with the sight of the foundling ward with too many children and too little air space; where the child often lies unattended for hours, surrounded by a mass of wet bedclothes and left to negotiate as best it may the contents of the nursing bottle.

*Diet.*—The excess of carbohydrates and starches in the food was formerly thought to be causative. Another theory is that the diet conducive to rickets is the one differing most in composition from the natural food of the child. The practice of meddling interference in breast feeding—i.e., giving the child additions to its diet which are unnecessary and of kinds unsuited to its age, particularly starch—has been thought by Still to be the cause of cases which he saw in England. Many in the profession are yet of the old opinion that a too small amount of fat in the dietary is a factor. But all we definitely know is that artificial feeding *per se* plays some part. Although breast babies do have it, rickets is by far more common in the bottle-fed. Insufficient food may play a secondary rôle in lowering nutritional standards, but as Grulee<sup>4</sup> has remarked, the severest forms of inanition which one so frequently encounters in early infancy rarely develop any rachitic changes; and this coincides with the author's experience. Faulty feeding may induce intestinal states such as intoxication which may or may not play a rôle. No one article in excess or in insufficient quantities has been proven causative, in spite of the volumes that have been written on the subject. One can at this time simply say that the *lack of breast feeding* is the cause of rickets, so far as diet is concerned.

Funk's hypothesis of the *absence of* an essential food factor, which he considers a *vitamin*, has caused rickets to be regarded by some as belonging to the so-called deficiency diseases. But the best explanation thus far given is that rickets is the *result of too much food*—usually artificial—exceeding the caloric requirements of the individual child and its ability to dispose of it. The one fact known is that with the appearance of rickets there is deficient calcium retention in the bones and increased loss of the mineral by way of the feces and urine. The amount excreted in this way may exceed the intake even on an adequate diet.

Undue confinement of the child, *lack of exercise*, and an *insufficient supply of fresh air* decrease the ability of the individual to handle the amount of food, which under these circumstances is excessive. Reference should here be made to the excellent theory of Pritchard,<sup>5</sup> who assigns the following principal methods of disposal of the excessive food ingested by the child: first, the excess may be stored up as glycogen or

\* Findlay's<sup>6</sup> investigations in the city of Glasgow lead him to state that the incidence of rickets is a question of economics. He believes that whatever the existing condition, the disease is fostered by bad housing, overcrowding, and absence of facilities for open air exercise.



fat, while the capacity for storage of nitrogen is markedly limited; second, combustion or oxidation to normal end-products of carbon dioxide, urea and water, with much waste of heat and oxygen; third, the production of incompletely oxidized products of combustion. By this third method the circulation is flooded with acids such as lactic, oxalic, uric, glycuronic, diacetic, beta-oxybutyric, and certain other organic acids which require alkalis and mineral elements from the tissues for their neutralization. Thus calcium and other bases are removed from organic union in the bones. As an accompaniment of this absorption of calcium, symptoms are present which we know as rickets. In overheated and poorly ventilated rooms, the child whose heat radiation is interfered with by too many clothes, and who lacks normal exercise, has very little demand for food; and very little fuel is burned. In the rachitic child evidences of this excessive combustion are found in the sweating, in the vascular dilatation, and in the bone demineralization.

The foregoing theory of the cause and the chemistry of rickets is offered as the best explanation thus far advanced. It should be possible therefore to cure incipient rickets by methods which will create in the child a demand and tolerance for a normal amount of food. Exercise, massage, handling, and life in the open air should make this possible.

**EXPERIMENTAL STUDIES.**—It has long been known that certain animals, such as monkeys and pups, that are kept confined in cages, develop rickets. In every zoölogical garden the disease is commonly known. In the laboratory of the University of Glasgow<sup>6</sup> it has been found that rickets may be produced in certain breeds of pups by simply confining them. On the same diet the animal allowed to run about does not develop it.

The symptoms which appear in animals deprived of their thymus gland are not similar to rickets.<sup>7</sup> There have been numerous experiments to determine the effect of the removal of the ductless glands on the development of rickets, but all are negative.

Many efforts have been made, but unsuccessfully, to find a proof of infectious origin for rickets. As not all infants under similar conditions develop rickets, it is necessary to find some explanation of what is the deciding factor. Absorption of intestinal toxins, lessened resistance after an acute infection, or bacterial infections of various kinds, might reasonably be the starting point for the rachitic process. Leila Jackson<sup>8</sup> in tests with experimental animal rickets found micrococci present in the bones, which she thinks significant if not positively causative. Koch believes that the ossification centers are reduced in resistance after infections such as whooping-cough or enteritis, and that these are sufficient to initiate the rachitic disease. Koch<sup>9</sup> states that chronic bone changes resulted after injection of *Streptococcus longus* into young laboratory animals; but these animals were kept in confinement.

The milk of nursing mothers, many of whom had rachitic children, was studied by Schabad,<sup>10</sup> who found that the calcium content progressively decreases during the lactating period. The amount in the milk

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**Definition.**—Rickets is a common nutritional and metabolic disease of the first two years of life, the chief characteristic of which is a failure to appropriate or retain calcium in the bones which become soft and deformed.

So-called fetal rickets (achondroplasia or dwarfism) is an entirely different disease. Tardy or late rickets is rare, appears in later childhood and will not be considered in this chapter.

**Etiology.**—PREDISPOSING CAUSES.—Rickets is a disease of civilized countries, as it is not found among primitive peoples living in the open sunshine of the tropics or in the frigid zones where the diet is largely made up of animal fat. Otherwise the disease is common the world over, but seems to be more prevalent in the temperate zones and in the cities. The essential predisposition seems to be in the unnatural style of living in our towns and cities to which the individual cannot adjust himself during infancy without definite metabolic disturbances.

Rickets, in America, usually begins and is more active in the winter and spring months, the higher incidence of the disease being in March. This is probably due to the cumulative effect of the almost constant housing and lack of sunshine at this time of year. The character of the winter food as regards its antirachitic content probably has no bearing on the causation of the disease but this is as yet not completely settled. It would seem from the recent successful attempts to impart antirachitic properties to foods by exposure to ultraviolet rays, that summer or autumn foods would possess more vitamin than they retain during the long winter months. Milk produced on summer pasture, however, gives no more protection against experimental rickets than does winter milk.

Age is a definite factor in the predisposition to rickets, as the greatest activity on the part of bone-forming tissue as well as the time of greatest

dependency or helplessness occurs in infancy. While rickets is slow in developing and the child is usually beyond the age of six months before the disease is clinically manifest, recent investigations show that early changes in the physiology and pathology of the bones begin as early as the first few months of life.

The influence of sex is not a definite one, although in the finding of rachitic sequelæ in older children, boys have been found affected more commonly than girls.



FIG. 1.—DEFORMITIES IN RICKETS.

Brother and sister, aged three and five years, members of an Italian family in which there is a younger child, all three with marked rachitic deformities.

An increased racial tendency to the disease undoubtedly exists among the negroes and Italians, especially those peoples transplanted from the tropic or warm climates. Antenatal influences may explain why one infant develops it and another does not. Few negro children in our cities escape the disease. In England, Gilmour found that the younger members of large families are more apt to show stigmata of rickets than are the older members.

It is recognized that the disease is generally one of the poorer classes. There are many reasons for this, such as the larger families and the absolute and relatively greater number of offspring among the poor, the

economic difficulty of giving the healthful attention needed and the lack of suitable living quarters. The greatest poverty, both as to percentage and degree, is in the crowded cities. This is reflected not only in the more frequent artificial feeding, with its poorer quality, lack of freshness and even in the quantity, but also in the air space of the house and the difficulty of securing pure fresh air out of doors. Bad hygiene and overcrowding in the cities is the lot of the poor.\*

*Influence of Diet.*—Too much carbohydrate and too little fat in the food were long thought to be the cause of the disease. It has been the clinical experience that much fat added to the diet does not cure rickets. A large amount of carbohydrate does lead to rapid growth and therefore might favor the development of rachitic changes in the bone. Undoubtedly many cases of rickets have been fed on an improper dietary so far as nutritional needs were concerned, but other infants similarly fed did not develop the disease. No infant would receive the restricted type of diet which causes rickets in experimental animals, as for instance the Sherman-Pappenheimer diet which consists of ninety-five per cent. white flour and five per cent. salts. Rickets is common upon all sorts of diets and absent in similar ones. Insufficient food may play a secondary rôle in lowering nutritional standards, but, as Grulee has observed, the severest forms of inanition which one so frequently encounters in infancy rarely develop any rachitic changes. It was found in a recent investigation carried on in the city of New Haven that poorly nourished infants seldom have rickets, while a slight degree of rickets is almost universal in breast babies who are unusually fat or growing rapidly. Hess found that rickets is not prevented by adding to the diet of the pregnant or nursing mother.

The natural supposition that whatever the food, it contains too little lime for the infant's needs, is not believed by anyone who has tried to cure rickets by high calcium diet, or who has observed that common dilutions of cow's milk still contain more calcium than the body needs. There are certain proprietary foods which have a mineral content below the body requirements, and if rickets were found only with such dietaries, the rickets-producing character of food could be proven.

Beginning with the work of Funk, most investigators now agree that an anti-rachitic vitamin, still unidentified, is essential as a factor in food which will prevent or cure rickets. Cod-liver oil and egg yolk are particularly rich in this fat-soluble vitamin.

Clinical rickets is by far more common in bottle-fed babies. Faulty feeding may induce intestinal states, such as intoxication, which may or may not play a rôle. No one article in excess or in insufficient quantities has been proven causative. Too much food, however, may have an influence in causing the disease in exceeding the caloric requirements of the individual child and its ability to utilize it.

\* Findlay's investigations in the city of Glasgow lead him to state that the evidence of rickets is a question of economics. He believes that whatever the exciting condition, the disease is fostered by bad housing, overcrowding, and absence of facilities for open exercise.

Foundlings' homes where infants are kept for long periods, and in which there is little air space and too much confinement, and lack of individual attention, and no best feeding, may predispose to the development of rickets.

*Hygienic Causes.*—The influence of hygienic factors, especially emphasized by British observers, is found in children who are unduly confined to their homes with lack of sufficient exercise and fresh air. Such conditions decrease the ability of the individual to handle the food which under such circumstances is excessive. In overheated and poorly ventilated rooms the child, whose heat radiation is interfered with by too many clothes and who lacks normal exercise, has little demand for food, and little fuel is burned. In the rachitic child evidences of this excessive combustion are found in the sweating, in the vascular dilatation and in the bone demineralization.

Whether or not the foregoing theory is correct, the recent discoveries of the value of natural and artificial ultra-violet rays place the hygienic theory on a sound basis. This does not exclude the influence of food as a factor.

*EXPERIMENTAL STUDIES.*—The amount of recent work done in the studies of rickets and the value of the discoveries along preventive and therapeutic lines have been enormous.

Mellanby was the first to discover that animals could be fed a diet which would produce rickets. At first dogs were used, but rats have proven to be more practical and are generally used in all metabolism laboratories. Sherman and Pappenheimer, McCollum and his co-workers have devised diets for rats which will prevent or cause rickets. The animals are killed and the bones studied for evidence of the disease. Some authorities question the identity of experimental and human rickets, but the bone pathology is much the same.

It has long been known that certain animals, such as monkeys and pups, confined in cages will develop rickets. In every zoölogical garden the disease is experienced. In the laboratory of the University of Glasgow it has been found that rickets may be produced in certain breeds of pups by simply confining them. On the same diet the animal allowed to run about does not develop it.

There have been numerous experiments to determine the effect of the removal of the parathyroid and thymus glands upon the development of rickets, but these are thus far negative for clinical rickets. The parathyroid has a marked influence upon the quantity of blood calcium.

Many efforts have been made, inconclusively, to find a proof of infectious origin for rickets. It is possible that such a cause may have a certain part to play.

The milk of nursing mothers, many of whom had rachitic children, was studied by Schabad who found that the calcium content progressively decreases during the lactation period. The amount in the milk cannot be increased by adding calcium to the mother's diet. On the other hand, fat in the milk progressively increases during lactation.

*Irradiation.*—The experimental studies showing the effect of the ultra-violet sun rays and the artificial rays from the mercury quartz lamp have been very extensive in the last few years and have added greatly to our knowledge of rickets. Huldshinsky first reported in 1920 the beneficial effects of quartz lamp therapy upon rachitic bones. How-

land and his associates in 1922 found that the phosphorus in the blood of rachitics was raised by quartz lamp exposure; both in experimental and clinical practice these findings have been constantly confirmed.

Hess has experimented with many food substances and when these are exposed to the quartz lamp rays they become protective against rickets in the experimental animal. He found that skin possesses the ability to store up anti-rachitic properties, for the feeding of portions of such skin to rats protected them. Milk powder, flour, spinach, lettuce and vegetable oils have been successfully activated by irradiation. Fresh milk does not acquire in this manner sufficient protective substances in the amount of milk that is usually fed. Hess's investigations in the study of cholesterol, which is normally present in large quantities in the skin, proved that this substance is susceptible to activation and becomes a depot for storing anti-rachitic substances. It has been found that negro children with their pigmented skin are as quickly cured by light rays as are white children.

Mellanby has suggested that the anti-rachitic effect from ultra-violet radiation of foods results from an increased vitamin content or that the vitamin may become more active. In the search for the method of the metabolic action produced by the ultra-violet rays, it has been thought by some observers that the rays are absorbed by the blood stream. The rays definitely increase the phosphorus in the blood in rickets and the calcium in tetany. Humphris found that ultra-violet radiation of rabbits caused an increase in the weight of their endocrine glands, the parathyroids showing the most marked increase. The author has recently found both the calcium and phosphorus to become normal or above after the daily subcutaneous injection of parathyroid extract in infants with tetany.

**METABOLISM.**—If fat is added to the diet of a rachitic child, the stools will show an increase of fat and there will be an increase in the calcium soap. Other factors than the presence of salts in cow's milk will influence the amount of calcium excreted. Bosworth believes that the calcium in the stool depends upon the form of the calcium intake, the activity of intestinal bacteria, and the amount of change from inactive to active calcium compounds by the hydrochloric acid of the stomach. Calcium is excreted by the bowel in combination with phosphorus as phosphate, and in combination with fats as calcium soap. Therefore phosphorus has much to do with calcium metabolism in health, while in rickets the combined salts are excreted in amounts to equal or exceed the intake. Little calcium but much phosphorus is excreted by the kidneys. That phosphorus has as much to do with the metabolism as has calcium has been found by Schabad and by Telfer.

The metabolism is influenced by the giving of cod-liver oil, causing the phosphorus in the blood to become increased in rickets, and the calcium in tetany as shown by Schabad. Phosphorus is also increased by the influence of ultra-violet radiation. Alfred Hess has noticed the variation in the phosphorus content of the blood with the curve of the ultra-violet radiation of the sun. The nature of the metabolic mechanism is not yet understood.

Findlay believes that the increased elimination is due to a digestive failure to absorb calcium and that this is the explanation of the disease. He thinks that lime is taken from the bones to supply the other tissues of the body. Most writers agree that there is poor absorption from the



FIG. 2.—RACHITIC DEFORMITIES.

Baby C. Seven months old child with marked frontal bosses, epiphyses and bowlegs.

intestine, or there is failure to appropriate the calcium which has been absorbed.

**Symptomatology.**—**PHYSICAL FINDINGS.**—Head sweating and restlessness are present early in its course. The infant is irritable, has a poor appetite, the bowels are constipated, the teeth slow to appear, the

fontanel is large and shows no evidence of closing, there is evidence of soft spots in the skull. The child makes little attempt to handle itself, does not hold up its head or sit erect, does not crawl or begin to walk at the usual age. The muscles are flabby and the child is anemic. Symp-



FIG. 3.—RICKETS.

Boy aged three years. Note bowing and twisting of legs and the flat foot.

These appear after the age of four months and during a period of several months progress to other marked evidences seen in the fully developed case. A study of the tissues and various regions of the body which are affected will best portray the disease.

*Muscular System.*—Of marked significance is the thinness, atony and flabbiness of the musculature. The muscles of the neck and back are sometimes unable to hold erect the head and spine. Functional curva-



tures of the spine result. There is distention of the abdomen, the so-called pot-belly, due to weakness of the abdominal muscles, to the thinned-out wall and distention of the intestines, to ptosis of the liver and other viscera, and to the eversion of the lower ribs. The arms and legs are flabby and do not support the child in attempts at use. The elbows and knees are easily hyperextended. The muscles of the feet are weak and do not support the arches.

*Ossseous System.* Change in the bone is sometimes first noted by trivial accidents which cause repeated fractures of the clavicle and the long bones. The most noticeable evidences in the bones are the epiphyseal enlargements at the wrist, knee and ankle. When palpated this thickening is found to be firm and not due to a deposit of fat. Beading of the ribs occurs in varying degrees. This rosary is due to a thickening of the anterior costal epiphyses and forms a somewhat irregular line running downward and backward parallel to the anterior ends of the ribs.

Increased abdominal tension produces eversion of the costal margin and above there is a depressed ring, Harrison's groove, due to retraction of the chest wall at the line of attachment of the diaphragm. The softened sternum yields to intrathoracic atmospheric pressure and various deformities occur such as pigeon-breast, barrel-chest, funnel-chest and flat chest.

The irregular shape of the head is brought about by undue softness and pliability of the skull, and by thickening or bosses in the frontal and parietal portions. The typical head of rickets is square, the forehead prominent, the top flat. Lateral flattening of the skull is present in a considerable number of cases. The anterior fontanel is large, asymmetrical and is late in closing. The angles of the fontanel run into sutures which with certain areas surrounding them are retarded in ossification. *Cranioleaves* consists of soft areas of parchment-like thinness. This symptom has become regarded as one of the earliest and most characteristic for diagnostic purposes, appearing as early as the third to fifth month of life. On percussion the parietal region will give a high-pitch (flat) resonance.

The lower dorsal and the lumbar vertebra are kyphotic and the processes prominent. Asymmetry and contraction of the pelvis occur, and remain to produce marked complications in the female pelvis during the child-bearing period.

The extremities show deformities of various degrees. In addition to the epiphyseal thickening already mentioned, the arms and legs are bowed laterally and anteriorly, and sometimes present spiral rotation and are shortened. Genu valgum and varum are frequent. The feet are pronated.

*Teething.*--Much emphasis has been placed upon the damage to the teeth. Such changes as poor growth, pitting and loss of the enamel, and early crumbling and caries have been ascribed to rachitic disease, but this is not proven. Such changes are seen in children, many of whom have not had rickets, and perfect teeth are seen in many cases who have

had active manifestations of the disease. Late teething however is the rule. The two lower central incisors which are the first to appear at the age of six to eight months are not much if any delayed, but the remainder of the deciduous teeth are three or more months behind time.

*Circulatory System.*—Pallor of the skin is evident. The veins are enlarged, especially on the scalp, forehead, thorax and the abdomen.

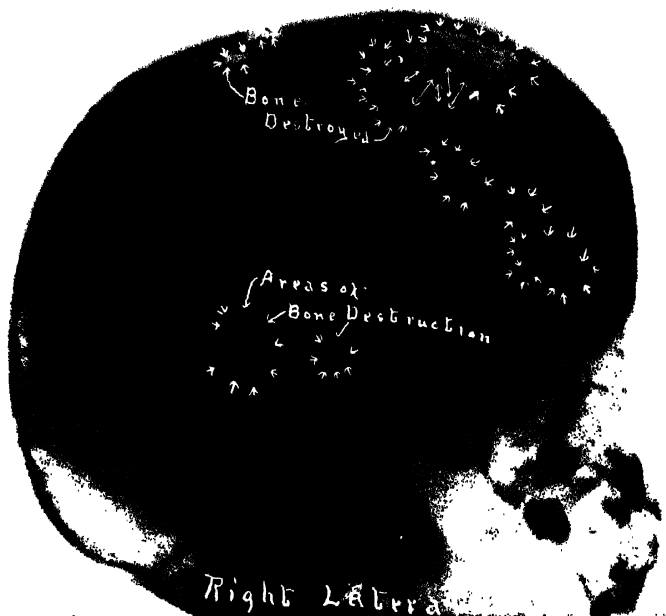


FIG. 4.—SKULL IN RICKETS.

Three-year-old child showing marked craniotabetic skull, particularly on top.

*Nervous System.*—The child is restless, especially at night, is irritable, and in some cases shows marked tenderness when handled. It has been questioned by Still and others whether tenderness is a true rachitic symptom, or rather an evidence of concurrent scurvy. The child occasionally has laryngismus, frequently has symptoms of tetany and convulsions. That the rachitic child has frequent convulsions during the period of the active disease is well known. In the author's experience rickets is usually not accompanied by other symptoms of tetany, such as facial irritability, spasm of the arm and leg muscles, and laryngismus. Head nodding, nystagmus, and in some cases a mild hydrocephalus are

sometimes associated with rickets. Various neuroses develop in the rachitic child, and there is probably a greater percentage of mental dullness than among non-rachitic children.

*Glandular System.*—Enlargement of the spleen is present in some cases, also a moderate enlargement of the superficial glands.

*Nutrition and Digestion.*—The rachitic child may be fatty and present little evidence of malnutrition, but in severe cases he does not long maintain an appearance of well being. The general muscular atony disturbs the digestive functions by limiting peristalsis, secretory and excretory functions. This lessened activity of the digestive organs, with the attendant constipation and toxemia, must play a part in the serious nutritional manifestations in advanced rickets.

*LABORATORY FINDINGS.*—*Blood Chemistry.*—The characteristic chemical finding in the blood is the lowered phosphorus content. The normal quantity ranges from four to five milligrams per hundred cubic centimeters of blood. In active rickets a content below 3.5 mg. should be regarded as diagnostic. In severe cases the phosphorus may be found as low as 1.5 mg.

Normal blood calcium ranges from 10.0 to 11.0 mg. per 100 c.c. of blood. It is generally regarded as little affected in rickets. Certain investigators however believe that rickets may be of two varieties; one with low phosphorus, and the other with low calcium.

Marked reduction in the calcium below 10 mg. should be regarded as indicative of co-existing tetany. Full term infants, on the other hand, have a surplus of blood calcium. One investigator has found an insufficiency of calcium in the premature. A slight difference in the chemical findings for normal white and colored breast-fed infants was noted by DeBuys and von Meysenbug in a study in New Orleans, the white infants having a phosphorus of 5.1 mg., calcium 9.7 mg., the colored a phosphorus of 4.2 mg. and a calcium of 8.9 mg.

*Microscopic.*—In the active stages there may be a reduction in the number of red cells to an average of about two million five hundred thousand. The monoblasts are increased in the well-developed case. The leucocytes are about ten thousand, and the differential unimportant. The anemia is secondary, with a decreased hemoglobin to as low even as forty-five per cent. in some cases. Intercurrent infections make it difficult to assign these blood changes to rickets.

*Feces.*—The analysis of the fecal ash shows that there is a marked increase in the calcium and phosphorus excreted through the stools.

*RÖNTGEN FINDINGS.*—The appearance of the bones under the roentgen ray is now depended upon for the minute and early diagnosis of early rickets. Normal infants have a clearly seen convex end of the long bones, with rounding of the corners. Lack of mineral in the bone with the decrease of density gives a lighter and more indistinct shadow. The earliest changes are seen at the lower end of the ulna and radius and may be present as early as two months of age. Such a condition may be cured in this early stage and not go on to marked pathological changes with clinical symptoms. Subsequent examinations when treatment is begun are used for determining the amount of healing that is taking place.

Cupping, fraying and irregularity of the ends of the shaft are characteristic, and their diameter markedly wider, their corners sharp or pointed. Because of the indistinctness of the bone outline the epiphyseal line between the shaft and cartilage is not so clear as in hard normal bones. Longitudinal stripes and trabeculae are seen running toward the shaft, these being more dense than the remainder of the bone. The shafts are narrower than in normal infants, due to subperiosteal resorption of the calcium. The long bones become sharply curved and show secondary deformities. Thickening at the extremities is most marked at the wrist, knee and ankle. The skull in advanced cases shows lighter areas corresponding to the craniotabes.

When treatment is effective the epiphyses begin to show mineralization at the centers of ossification. This begins just above the end of the shaft. Later the width of the long bones increases, and the lighter shadows in the skull are replaced by a shadow of uniform density. Throughout the affected osseous system the outline of the bones becomes clearer as cure proceeds.

**Diagnosis.**—It is important that mild and early rickets should be recognized, as it is a curable disease, and at such a time deformity and serious manifestations may be prevented. The child should be watched for evidences of head sweating, late teething, backwardness in holding up the head and in handling itself, irritability, restlessness, constipation, persistent fontanelle and sutures. The diagnosis is easy when to these symptoms are added prominent frontal and parietal bones, pot-belly, flabbiness of the muscles and weakness of the extremities, or pseudo-paralysis. X-ray changes showing sharp curving of the shafts and widening of the ends of the long bones are valuable confirmatory signs.

The thick wrists and the beading of the ribs furnish the earliest and most marked diagnostic signs. One must not mistake fat wrists for an enlargement in the diameter of the epiphysis, nor should the physiological thickening of the costochondral junction be mistaken for the true rachitic rosary.

Softening of the structures of the bony framework of the chest is found in some non-rachitic infants who are atrophic. When there is difficulty in making a diagnosis the finding of a low phosphorus content of the blood will be of marked assistance.

**Complications.**—Respiratory infections are common in the rachitic child. Resistance is lowered by the general weakness, the anemia, the impairment of the respiratory effort, due to deformity of the thorax and flabbiness of the chest muscles. The thorax is soft and yielding. Such impairment of function must lead to interference with proper respiration and the consequent lowered resistance both in the respiratory tract and throughout the body. Howland and Park believe that severe chest deformities are a menace to life, death occurring from mechanical respiratory failure. Bronchitis and pneumonia find suitable ground for development in such children. Fractures of the bones, especially of the clavicle, are common.

Dilatation of the stomach and colon are marked in certain cases.

Constipation is common, though it may alternate with periods of diarrhea and other evidences of intestinal indigestion.

**Sequelæ.** One has only to examine older children and adults to find the trail of early rickets. The deformities which hold over into later life are flat foot, knock-knees, bowlegs, stunted stature, deformed and narrow pelvis, ponderous abdomen, ptosis of the viscera, narrow, flat, and pigeon chest, spinal curvatures, crumbling teeth, flat-topped and square-shaped heads.

Out of 100 rachitic children reported by Horwitz 64 per cent. had knock-knees, 28 per cent. bowlegs and 8 per cent. weak feet.

The percentage of school children showing deformities and other rachitic stigmata is considerable in our large cities. Among 1,000 London children in the East End of that city 80 per cent. showed evidences of rickets. Dick found in examining 586 cases that 58 per cent. had defective permanent teeth. Of these, hypoplasia or defective calcification was found in 20 per cent., and in 38 per cent. there was marked caries. The order of frequency in caries is the first lower molar, the first upper molar, one or more lower and upper premolars.

Fixed scoliosis is a bone deformity and is usually of rachitic origin. This is found early in school life and is not the result of habit. Kirsch found that 20 per cent. of the children examined gave this evidence of rickets.

Permanent digestive impairment, frailty of the general health and neuropathic states are seen in rachitic individuals.

**Association with Other Disease.**—Rickets has nothing in common with scurvy, though they are sometimes confused by those unfamiliar with both diseases; and undoubtedly the two co-exist occasionally. A case of rickets which has marked tenderness and either superficial or periosteal hemorrhage should be counted as having scorbutus also.

Any child who has "gone off its legs" may have its disability mistaken for rheumatism, infantile paralysis, syphilis, or scurvy. There are in rickets no paralytic phenomena.

Rachitic kyphosis may be mistaken for tuberculosis. The usual disappearance of the deformity in the prone position, the absence of characteristic X-ray findings, and the presence of general rachitic symptoms, will be sufficient for a diagnosis.

Other rarifying bone diseases are unusual at the age in which the florid manifestations of rickets are present.

Recent studies are separating infantile tetany and spasmodophilia from rachitis. Undoubtedly they frequently co-exist. Convulsions are common in rickets, whether due to the presence of tetany or inherent to certain cases of rickets. The calcium in the blood of infants with tetany is much reduced.

Scorbutus was at one time not separated from "acute rickets." Rachitis and scorbutus are frequently associated, but we know them as separate diseases.

That premature infants will develop rickets has been recently shown. In seventy cases of premature and twin children Huenekeus reported

that rickets appeared in 92 per cent. This is due, he thinks, to a deficiency of calcium at birth. Other factors than congenital deficiency may be found in the immaturity of the child, the deficient intake of food, and the lack of air and handling.

Hereditary syphilis is likewise often co-existent with rickets, a fact to be expected from the frequency of both diseases. It is reasonable that in certain cases lues may make easy the development of rickets.

**Treatment.**—**PROPHYLAXIS.**—The prevention of rickets in the individual child is a much simpler matter than the public health problem of rickets-prevention. With the recent knowledge that has come with the study of the disease, it is to be expected that marked symptoms of rickets will seldom be seen in the child who is examined at sufficiently close intervals. The opportunity for a complete dietary, for prevention of many infections, and for plenty of fresh air and hours of sunshine each day is a matter of attainment by families who have the advice of competent authorities. A diet which is adequate will consist of breast milk when possible, or of cow's milk otherwise. Cow's milk is now given in more concentrated formulas. Digestion is made easier and more complete by souring the milk with lactic acid organisms, commercial lactic acid, or hydrochloric acid. Egg yolk contains antirachitic properties and may be begun at three months of age. Sugar, fruit juices and cereals may be added to the diet as indicated. Cod-liver oil administration is becoming a routine in the practice of those who deal with infants. It should be given in sufficient doses of a teaspoonful twice daily. That the beneficial effects of the sun's rays will not filter through the closed windows of a sleeping porch or room is not so commonly known. Infants as a rule are still much overdressed in winter and even in summer.

The community prevention of rickets has not as yet been begun except in an experimental way in a few cities. Hess and others in the New York Department of Health, Eliot, Park and others in the New Haven organizations have made valuable contributions concerning the presence of rickets and its prevention on a large scale. Much of the population is without the advice of medical authorities. It will take the combined efforts of physicians in their practice, the public health organizations, the universities, the dispensaries, and child-welfare organizations to put into effect the necessary measures.

**CURATIVE.**—The essentials of therapeutic treatment which should be emphasized are sunshine, cod-liver oil and adequate diet.

The beneficial effects of the sunshine are due to the ultra-violet or short rays. They are not effective through window glass. The infant should receive a sun bath twice daily, which may in severely cold weather be given with the child held or lying in bed near the open window, during the late forenoon and early afternoon. In cold weather only the face need be exposed, and the body covered with white, loosely woven clothing. In reasonable weather the infant should be taken out of doors beginning with an exposure of a half hour and increasing the time until the skin attains a pigmentation which is the measure of therapeutic efficiency. Although there are long periods in the winter and spring

months when little sunshine is present, the out-door air is still of value. The author has seen children become tanned through days of exposure to the winter wind and air of the roof garden of the hospital, and their well-being was as noticeable as at other periods of the year. The rachitic child is usually fat and can stand cold weather better than poorly nourished babies. The importance of light in the human organism is as great as for plant life.

Artificial ultra-violet rays are not yet available for much of the population. In severe rickets it is desirable to make use of exposure to the quartz lamp, especially during gloomy and unsuitable weather, as the cure is hastened thereby. Bone calcification progresses steadily as shown by radiograms from week to week. With proper protection to the eyes and graduated doses to increase the skin tolerance there is no contraindication to artificial irradiation. Its benefit is now well established and its use recommended.

*Medication.*—Sufficient emphasis needs to be placed upon the amount of actual **cod-liver oil** given infants in the prevention and cure of rickets. Beginning with one month of age **one-half teaspoonful** of **pure oil** should be given twice daily and after the second month a teaspoonful is given. Emulsions or dilutions should therefore be administered in sufficient quantities to insure this dosage of actual oil. As large doses as a dessert-spoonful twice daily have been successfully given after the fourth month in the active disease when needed.

**Phosphorus** may be added to the oil in a dosage of  $1/200$  to  $1/500$  of a **grain** (0.3 mg. to 0.12 mg.). A convenient form of administration is the official oil which contains  $1/100$  of a grain (0.6 mg.) in each minim. Phosphorus has been proven to increase the calcium retention in the bones and its use seems rational.

Symptoms which require special treatment are nervousness and convulsions for which **hot baths**, **chloral** and **bromid** are indicated. **Warm baths** are a useful form of exercise for the infant and should be combined with **massage** once daily. These have a sedative effect. Constipation will be lessened by the varied diet, the cod-liver oil and an occasional dose of a laxative such as mineral oil.

The child should be given **iron** for the anemia, a convenient form of which is the **soluble citrate** given in **one-half to two grains** three times daily. Any measure improving the general body tone and lessening the deformity should be instituted. The addition of lime salts to the diet does not increase the calcium in the blood.

*Diet.*—In the early months of life should rickets appear it is well to continue the breast feeding and give additional food according to the needs of the child. It is probable that the acid-containing foods, especially lactic acid buttermilk, the U. S. P. lactic acid formula of **Marriott** and the hydrochloric acid formula of **Faver**, have some antirachitic value. They at least supply the infant with a complete milk dietary which requires no dilution in most cases. The **yolk of egg** possesses some antirachitic vitamin and should be given either raw or coddled. This may be put in the bottle or fed with a spoon and begun both as a help in

the prevention of the disease after the third month of age or at any time in the developed case. Fruit juices, vegetable soup and purée, cereal, sugar, butter, and scraped meat should be given at an appropriate age. The careful feeding of the infant now warrants a broader variety than was the custom ten years ago. Such a diet with the addition of cod-liver oil will be preventive and curative.

**Prognosis.**—The outcome of rickets is good as to life. Death may occur from some acute respiratory complication or from spasm of the larynx, from convulsions or other manifestations of severity.

No figures are obtainable as to the death rate, but *death is exceedingly rare in simple rickets.*

Although the deformities are marked and even grotesque in some cases, such as those seen frequently among the negroes, it is remarkable how much spontaneous improvement will occur. The writer remembers a negro child with corkscrew legs who was again seen at the age of puberty. There was little evidence, except flat-foot, that rickets had ever occurred. However, it is usual to find a moderate amount of chest deformity, depression at Harrison's groove, prominent belly and marked flat-foot. That the neuropathic tendency of rickets sometimes persists through later life is probable. The duration of rickets is variable. Active rickets is seldom carried over beyond the age of two or three years.

**Pathology.**—GROSS CHANGES.—The essential anatomical lesions are found in the osseous system. They are, in brief, the more than physiological absorption of bone tissue, and the simultaneous retardation of calcification. The resulting bone tissue is spongy and has been called *osteoid tissue*. The decrease in the strength and firmness of the osseous system reduces the general stability of the body frame. Marked deformities occur. The long bones are sharply curved. The sternum and ribs are distorted so that in the severe cases the thoracic cavity shows little resemblance to the normal contour. The spinal column as a whole may show curvature in any direction and the vertebræ themselves may take part in the general bone deformity. The pelvis is often contracted and shallow, although this is not in evidence during childhood. Cranial bosses, craniotabes and changes in the general contour of the head are results of the rachitic processes of bone thickening, absorption and softening. The average circumference of the rachitic head is one and one-fourth inches above the normal at the age of from 5 to 6 years. The size and bulging shape of the forehead are suggestive of mild hydrocephalus, but this is not proven. The fontanel remains open as a result of the delay in ossification. It may be open till the third year.

The characteristic osseous enlargement is found at the epiphysis, where there is irregular thickening caused by cartilage proliferation and by a mass of irregularly formed new bone at the diaphyseal end. The long bones, in severe cases, are spindle shaped, with wide flaring ends, and the shaft is greatly reduced in diameter from bone absorption.

Extrinsic causes aid in the production of the deformities, such as: the superimposed weight of the body upon the yielding body frame, muscu-



lar traction, for instance at the diaphragmatic insertion, atmospheric pressure within the thorax, posture and pressure from lying or being held. Some of the deformities of the cranium are the result of pressure—the intracranial tension and the venous grooving under the scalp.

**MINUTE CHANGES.**—The proliferation of cells in the cartilage and under the periosteum proceeds with abnormal rapidity. In the zone of proliferation the cells are piled up irregularly. The cartilage cells are hypertrophied, there is lack of the usual uniform arrangement in the rows of cells, and the vascularity is greatly increased. Vascular medullary spaces are developed in the zone of ossification where the calcification is irregular and osteoid tissue is formed. Throughout the bone there is the same hyperemia, abnormal stimulation of absorption, irregular arrangement of cartilage and bone-forming cells, with areas of incompletely calcified portions invaded by areas of cartilage proliferation.

**CHEMICAL CHANGES.**—The calcium content of the tissues of the body other than bones is not affected. Bones usually contain 65 per cent. of mineral elements, but in rickets these may be reduced to as low as 25 per cent. The pre-existing bone becomes therefore largely demineralized, and there is a failure to lay down sufficient lime salts in the newly formed bone.

**OTHER CHANGES.**—Pathological changes have been found in the muscles and viscera. That these are the result of rachitic disease is not proven. The muscular fibers are said to be thin and immature, the nuclei increased in number, and the longitudinal striations distorted. In some cases there is much fat deposited, and more or less degeneration of the fibers. The spleen may be enlarged and show hyperplasia of the pulp and follicles, eventually becoming fibrous. The lungs, in severe cases of thoracic deformity, show areas of atelectasis and emphysema. The heart may be flabby and present hypertrophy. Fatty degeneration of the liver may be present, but definite enlargement due to rickets is not yet proven.

Investigations lead the New Haven investigators\* to question whether the presence of a slight amount of rickets may not be physiological or normal for infants living in such a climate and in the present state of civilization. Education in child hygiene and the supervision of the care of the infant will show marked benefits, at least among teachable individuals. Provision for the maintenance of maternal nursing necessitates the retention of the mother in the home. Withdrawal of mothers from industrial pursuits is a problem that may never be solved, but in the light of our present knowledge of rickets, no person other than the mother can be found in the families of the masses who will see that the child gets the hygiene and dietary care that is necessary.

\* The author is indebted to Dr. Martha M. Eliot, New Haven, for her early report on the rickets-prevention work which is being carried on in New Haven by the U. S. Children's Bureau, the Pediatric Department of Yale School of Medicine, the City Health Department, the New Haven Medical Society, the Public Health Department of Yale and the Visiting Nurses' Association.

## CHAPTER IX

### SCURVY

BY EDWARD B. VEDDER, A.M., M.D.

Definition, p. 161—History, p. 161—Etiology, p. 163—Symptomatology, p. 166—Diagnosis, p. 170—Association with other diseases, p. 170—Pathology, p. 171—Treatment, p. 172—Prophylaxis, p. 172—Medicinal treatment, p. 174—General management, p. 175—Prognosis, p. 176—References, p. 176.

**Definition.**—Scurvy is caused by faulty metabolism, and is now believed to be due to a deficiency in the diet of some unknown substance belonging to the group of substances that are frequently called vitamins. This antiscorbutic vitamin is present in fresh fruits, fresh vegetables, and to a lesser extent in fresh meat. The prolonged deprivation of these articles of diet is the cause of the disease. Scurvy is characterized clinically by great debility, by a marked tendency to hemorrhages into various tissues, associated with changes in the bones resulting in softening and fragility.

**History.**—There is some reason to believe that scurvy occurred among armies in ancient times, both because the diet of the soldiers was probably deficient then as well as later, and because of passages from certain writers. Thus Pliny<sup>1</sup> says that the Roman Army under Caesar Germanicus after an encampment of two years in Germany, suffered with a disease in which the teeth dropped out and the knees became paralytic. They discovered a remedy for it in a plant called "*herba Britannica*." Similar references may be found in the works of Hippocrates, Celsus, Galen, and Strabo. Of all of these, it may be said that the descriptions of the disease were too vague to identify it with certainty as scurvy. According to Lind, the first good description of scurvy is to be found in a history of Louis IX by Le Sieur Joinville, who wrote of the disease in the Christian army in Egypt in about the year 1260.

Scurvy was probably unknown among sailors of ancient times because their voyages were all short. With improvement in navigation and the discovery of the Indies, long voyages were performed, and scurvy promptly commenced to appear among the seamen. Vasco da Gama first made a passage to the East Indies by the Cape of Good Hope in 1497, and 100 out of his 160 men died of scurvy. The first account of scurvy among seamen is to be found in the description of that voyage. The nature of the disease was not understood then or for several hundred years thereafter, and scurvy continued to appear at various times and places, and was particularly prone to occur among seamen and soldiers.

The ravages of scurvy under such circumstances are indicated by the following quotations:

(1) *The second voyage of James Cartier to Newfoundland in 1535.*

“In the month of December, we understood that the pestilence was come upon the people of the *Stadacona* to such a degree that before we knew of it above fifty of them died. Whereupon we charged them neither to come near our forts, nor about our ships. Notwithstanding which, the said unknown sickness began to spread itself amongst us after the strangest manner that was ever heard of or seen: insomuch that some did lose all their strength and could not stand upon their feet. Then their legs did swell, their sinews shrunk, and became as black as a coal. Others had also their skin spotted with spots of blood of a purple color. Their mouths became stinking, their gums so rotten that all the flesh came away, even to the roots of their teeth, which last did also almost fall out. This infection spread so about the middle of February, that of a hundred and ten people there were not ten of us in health. Twenty-five of our best men died, and all the rest were so ill that we thought they would never recover again.”

(2) *Lord Anson's voyage around the world in 1740-1744.*

On the 18th of September, 1740, a squadron composed of five men-of-war sailed under the command of Commodore Anson from England to cruise about the world. But one of these ships, the *Centurion*, and but five per cent. of the personnel returned to England after an absence of four years. Terrible as were these sufferings, they were no unusual accompaniment of long voyages in those days. The quotations that follow are taken from the account of this voyage by Richard Walter.

“Soon after passing straits *Le Maire*, the scurvy began to make its appearance among us. And our long continuance at sea and the fatigue we underwent, and the various disappointments we met with had occasioned its spreading to such a degree that at the latter end of April there were but few on board who were not in some degree afflicted with it. And in that month no less than forty died of it on board the *Centurion*. But though we then thought that the distemper had arisen to an extraordinary height, and were willing to hope that as we advanced to the Northward its malignity would abate, yet we found, on the contrary, that in the month of May we lost double that number. And as we did not get to land till the middle of June, the mortality went on increasing so that after the loss of above 200 men, we could not at last muster more than six foremast men in a watch capable of duty.

“But a most extraordinary circumstance, and what would be scarcely credible upon any single evidence, is, that the scars of wounds that had been for many years healed, were forced open again by this virulent distemper. Of this there was a remarkable instance in one of the invalids on board the *Centurion*, who had been wounded above fifty years before at the battle of the Boyne. For, though he was cured soon after and

had continued well for a great number of years past, yet, on his being attacked by the scurvy his wounds in the progress of the disease broke out afresh, and appeared as if they had never been healed. Nay, what is still more astonishing, the callus of a broken bone, which had been completely formed for a long time, was found to be hereby dissolved, and the fracture seemed as if it had never been consolidated.

"The havock which this dreadful calamity made in those ships was truly surprising. The *Centurion* from her leaving England, when at this Island (Juan Fernandez) had buried 292 men and had but 212 remaining of her complement. The *Gloucester*, out of a smaller complement, buried the same number and had only 82 alive."

Scurvy was frequent in besieged towns especially in the winter and spring. In the siege of Breda in 1625 an account was taken of the number of patients, and 1608 were found to be suffering from scurvy. Bachstrom states that at the siege of Thorn in Prussia in 1703, above 6,000 of the garrison, besides a great number of the inhabitants, died of this disease, and the surrender of the town was due more to the scurvy than to the bravery of the besiegers. Such instances might be multiplied indefinitely. According to Surgeon Tripler,<sup>2</sup> in 1809 we lost 600 men on the lower Mississippi from scurvy, and in 1820, when a large force was sent to Council Bluffs and wintered there, we lost 168 men from scurvy and there were more than 500 cases at the post. Scurvy continued at many Western frontier posts until the Civil War, and during that war there were 30,714 cases among the white troops alone with 383 deaths, and the rate was higher among the colored troops.<sup>3</sup> In the French army in the Crimea from April, 1854, to June, 1856, with an average of 86,740 men there were 23,250 cases of scurvy and 645 deaths from that disease, irrespective of those who died after being sent home. In more recent years scurvy has been rarer in armies, though Hoff states<sup>4</sup> with regard to the Russian troops in the Russo-Japanese War that "the 1,180 cases of scurvy with ten deaths represent but a small proportion of those more or less affected with the scorbutic taint. I learned from many sources that scurvy modified the course of both medical and surgical cases, and I have actually seen cases of typhoid fever with marked scorbutic symptoms."

**Etiology: Development of Knowledge.**—Cockburn, in 1696,<sup>5</sup> was one of the first to point out both the cause and the cure for scurvy. "The scurvy being generated by the salt provisions altogether unavoidable at sea, makes one of the constant diseases in navies. Refraining from the sea diet and living upon green trade (as it is called) on shore, proves an absolute cure. It is worthy observation how suddenly and how perfectly they recover of this distemper by eating greens, namely, coleworts, carrots, cabbages, turnips, etc. Men put on shore in the most pitiful condition that can be imagined, are able in three or four days, by means of this food only, to walk several miles into the country."

Bachstrom, in 1734, also pointed out that the primary cause of the disease was the abstinence from fresh vegetable foods, and that, although

other secondary causes might play a part, recent vegetables were an effectual preventive. Kramer described the scurvy among the German soldiers in Hungary in 1735. He insisted that the disease was not infectious. "No officers are seized with it, and only the regiments of such nations who use too gross a diet, namely flesh and the grosser farines, coarse heavy bread and puddings." He tried all antiscorbutic remedies that had ever been recommended and found them all useless except fresh green plants.

Lind<sup>6</sup> in 1753 published a work which ran through three editions, and which is to-day one of the most important works on scurvy. Lind pointed out clearly that the disease is not infectious, and that general experience indicated that fresh vegetables are effectual in preventing and curing the disease; but insisted on the importance of certain predisposing causes including moisture, cold and fatigue which are now known to be of little importance. He emphasized the great value of oranges, lemons and limes as a cure for the disease, and recommended carrying these juices on long voyages as an antiscorbutic.

Blane<sup>7</sup> in 1785 repeated this recommendation and persuaded the authorities to give it a systematic trial. In 1793 the *Suffolk*, a flagship of 74 guns, made a voyage of nineteen weeks to the East Indies without touching at any port. Each man was given daily three-fourths of an ounce of lemon juice with two ounces of brown sugar. On the arrival of the *Suffolk* at Madras, there were only fifteen on the sick list, and not a single case of scurvy, a most remarkable result for those days. This experiment was so impressive that lemon juice was introduced as a regular item of the naval ration in 1795 by order of the Admiralty. One ounce was issued daily to each man. This single measure eradicated scurvy from the British navy, and was one of the greatest sanitary improvements of all times. According to Budd,<sup>8</sup> in the year 1780 there were 1457 cases of scurvy admitted to Haslar hospital. In 1810, one of the physicians of that hospital stated that he had not seen a case in seven years. Scurvy, however, continued to be rampant among the seamen in the mercantile service where lemon juice was not issued, until similar regulations as to the issue of lemon juice were formulated by the British Board of Trade in 1865. Scurvy was then similarly obliterated from the mercantile marine.

With the discovery of the cause of scurvy and the introduction of fruit juices as preventives, the disease became comparatively rare and little scientific interest was displayed in the determination of the exact substance that was deficient in a scurvy-producing diet. In 1843 Garrod<sup>9</sup> thought the deficient element was potassium. He pointed out that, although acid fruits are highly antiscorbutic, the extracted acids are not so, and that fresh milk, which when used in sufficient quantity, will prevent scurvy, contains no organic acid. Garrod found on analysis that foods shown to be antiscorbutic contain a large amount of potash, and that in scurvy the blood is deficient in potash, although there is no decrease in the amount of the other inorganic salts. Garrod's conclusions were hypothetical and unproved, but for many years potash was

largely used in the treatment of scurvy, with very poor results. Potassium nitrate was tried on scorbutic convicts en route to New Zealand, and Bryson, who reported the results of the experiment, thought it worse than cruelty to persist in the exhibition of this salt either as a prophylactic or a means of cure.<sup>10</sup>

No real advance in knowledge of the etiology of scurvy was made until 1907, when Holst and Froelich<sup>11</sup> found that a diet of various grains and bread produces a disease in guinea pigs that corresponds in all details to human scurvy. Scurvy could not be produced in guinea pigs on a one-sided diet of fresh cabbage, fresh carrots or fresh potatoes, although they may lose from 30 to 40 per cent. of their body weight on this diet. The disease was again produced on a diet of dried potatoes.

Since the condition produced in the guinea pig corresponded clinically and pathologically with human scurvy, and since the same one-sided diets that produce scurvy in guinea pigs have repeatedly produced scurvy in man, and since these results have been confirmed many times by independent investigators, there can be no doubt that the guinea pig is a suitable animal for the experimental study of scurvy. That so little progress has been made since 1907 in elucidating the nature of the scurvy vitamin is largely because of the lack of interest in this subject owing to the comparative rarity of human scurvy during these years.

In a later paper Holst and Froelich<sup>12</sup> showed that vegetables lose their antiscorbutic properties through long drying, and that cooking to 110°-120° C. (230°-248° F.) destroys the antiscorbutic property of cabbage. They also found that they could extract the antiscorbutic substance from cabbage with acidulated water or acidulated alcohol, and that it could not be extracted by cold petroleum ether. Hess and Unger<sup>13</sup> have also shown that the protective substance in orange juice is soluble in 95 per cent. alcohol. Holst and Froelich also indicated that the substance is dialyzable, though their experiment on this point was not conclusive.

The protective substance or vitamin of scurvy is therefore water soluble, alcohol soluble and ether insoluble and probably dialyzable, in which characteristics it resembles the beriberi vitamin. It differs from the beriberi vitamin in the fact that it is destroyed by drying, is not adsorbed by kaolin and is even more susceptible to heat. Holst and Froelich found that fresh cabbage juice loses the greater part of its antiscorbutic properties if heated for ten minutes to 60°, 70° or 100° C. (140°, 158° or 212° F.). The beriberi vitamin withstands long heating to 80° or even 100° C. (176° or 212° F.) in most extracts or food stuffs.

The scurvy and beriberi vitamins also differ remarkably in their incidence in nature, as has long been known and has been well pointed out by Chick and Hume.<sup>14</sup> The whole wheat or rice grains, the polishings removed from these grains in milling, dried peas and beans, and yeast all afford protection against beriberi, but are totally devoid of antiscorbutic vitamin. On the other hand, fresh potatoes, onions, cabbage and fruit juices which have little or none of the beriberi vitamin, are rich in antiscorbutic properties. All of these observations indicate that,

although the beriberi and scurvy vitamins are similar in some respects, and may very probably belong to the same class of chemical substances, they cannot be identical.

**Symptomatology.**—THE DEPLETION PERIOD.—As scurvy is a deficiency disease, the term incubation period is a misnomer. The depletion period is the time that elapses between the institution of the faulty diet and the first definite symptoms of the disease. As usually observed in man this is from four to seven months. It is shorter among susceptible individuals and among those entirely deprived of scurvy-preventing foods, and longer among resistant individuals and among those who receive a small but insufficient amount of antiscorbutic foods. Thus in Lord Anson's voyage around the world,<sup>15</sup> his squadron sailed September 18, 1740, and scurvy appeared among the crew in April, 1741. Koren<sup>16</sup> reported the case of a fanatical vegetarian who lived exclusively on bread and water and developed scurvy after seven and a half months. Colonel Hchir (*Mesopotamia Report*, 1917, x, 41) considers four months the minimum time in which scurvy will appear among Indian troops on service. There are numerous instances in the literature of voyages or sieges in which scurvy appeared after a few weeks. But investigation of these cases will show that the voyage or siege began in the spring and that the victims had been largely deprived of antiscorbutic foods for a considerable period during the previous winter, or immediately prior to the time when the absolute deprivation set in. Infantile scurvy appears only after several months of artificial feeding and is very rarely seen among children less than six months old. Younger animals are more susceptible to experimental scurvy than older animals, so that we would expect the depletion period to be longer in adults than in children.

**MODE OF ONSET.**—Before the onset of definite symptoms of scurvy, there is a period of debility and weakened resistance to disease. This has been called "latent scurvy." The earliest symptoms are loss of weight with languor, lassitude, dizziness on standing and fatigue on the slightest exertion, and a pallid or yellowish complexion. In other respects, the patient appears to be in his normal condition at this time: he eats heartily and his bowels are usually regular.

Soon in addition to the fatigue there are dull aching pains in the legs and feet. This pain may be referred to the bones or to the larger joints, and during the Civil War soldiers so affected were often at first diagnosed as cases of rheumatism.<sup>3</sup> Instead of pain the patient may complain of stiffness of the knees or feebleness of the leg muscles. Diarrhea is often a symptom of incipient scurvy, but is by no means constant at this stage, though when fully developed scurvy is frequently associated with diarrhea.

**GENERAL SYMPTOMS.**—*The Hemorrhagic Diathesis.*—Soon after this early stage the tendency to interstitial hemorrhage becomes marked, and the symptomatology of the disease depends chiefly upon the number, amount and location of these interstitial hemorrhages. It will be understood that they may occur into any tissue of the body, but the more usual situations will be described.

*The Gums.*—The changes in the gums are one of the most constant, early and characteristic features of the disease, though they are not invariably present. The gums swell and are very red and spongy and are apt to bleed upon the slightest provocation. This swelling is probably due to hemorrhage into the tissues of the gums. The swelling begins first and is most intense in the lower jaw, usually around the molar teeth and progressing forward. The swelling increases gradually until the gums may rise to the level of the teeth, especially the lower molars. At first red, the gums later become livid, and as the older writers used to say, "fungous." The swollen and spongy tissue ulcerates and breaks down, often sloughing away until the necks of the teeth are left bare. The teeth become loose and often fall out, partly because of loss of gum tissue, and partly because of softening of the bony structure of the alveolus. As the result of this condition of the mouth, mastication may become impossible and the diet is restricted to soft food and liquids. The breath becomes exceedingly offensive.

*The Skin.*—The characteristic hemorrhages appear first as petechial spots. Later these spots become larger, "from the bigness of a lentil to that of a hand-breadth and bigger." These subcutaneous hemorrhages are more common on the legs and thighs, but may appear on the arms and body. They seldom occur on the face. The spots may be of all colors; red when the effusion first occurs, later becoming purplish or livid, and varying from greenish blue to dusky yellow as they become absorbed. These subcutaneous hemorrhages may occur frequently or at any time during the course of the disease, so that the limbs may be covered with blotches in all stages of evolution. The spots so produced are not painful or tender on pressure unless there is at the same time effusion into the muscles.

In many cases the legs become edematous, at first swelling in the evening and returning to normal in the morning. Later the edema may be marked over the entire leg, which pits on pressure.

Still later in the course of the disease there is a tendency for these hemorrhagic areas to ulcerate particularly when on the legs. The slightest scratch or other injury at this time may be sufficient to cause the formation of such an ulcer. The edges of the ulcer are swollen and livid, and the bottoms are covered with exuberant granulations. Lind<sup>6</sup> describes these granulations as a "soft bloody fungus," and says, "it often arises in a night's time to a monstrous size, and though destroyed by caustics or the knife, in which case a plentiful bleeding generally ensues, it is found at the next dressing as large as ever." It is particularly important that these ulcers be not mistaken for the ulcers of syphilitic origin, for mercury is very badly borne by scorbutics, almost always causing salivation and exacerbation of the swelling of the gums, and it has been known to cause the death of the patient.<sup>17</sup>

*The Muscles.*—There is also a tendency for diffuse interstitial hemorrhages into the muscles, particularly the muscles of the leg and thigh and more especially around the knee joint. The stiffness and weakness of the knee joints early in the disease is probably caused by this effusion



of blood into the surrounding muscles and tissues. When these hemorrhages are large they cause swelling of the legs, and as the blood subsequently coagulates the knee becomes fixed in a flexed posture. The ankle may be similarly affected. Finally, there may be a brawny hemorrhagic infiltration of both muscles and subcutaneous tissue. These muscular hemorrhages cause violent and racking pains, and tenderness on pressure, and walking becomes impossible because of the disability and the pain.

*The Bones.*—Hemorrhages are prone to occur under the periosteum, particularly of the tibiae, and the medulla becomes infiltrated with numerous small hemorrhages. The shaft of the bones becomes spongy and fragile. The bones most frequently affected are the tibia and femur, particularly near the knee and ankle joints, the ribs and the lower jaw. This condition causes continuous pain and tenderness on pressure. There is a tendency to spontaneous fracture and the callus of repaired fractures may undergo absorption. The ribs may become separated from the costosternal junction, and the epiphyses of the long bones may become separated, particularly at the knee joint. The frequent racking pain which scorbutic patients often experience in the limbs, back and chest is probably due partly to the effusions into the muscles and partly to these bone changes.

*Hemorrhages.*—Scorbutic patients are liable, particularly in the late stages of the disease, to profuse hemorrhages from various parts of the body, such as the nose, the gums, from preëxisting ulcers or from the bowels. Hemoptysis, hematuria and hematemesis occur uncommonly. Bleeding from the bowels is relatively common. Hemorrhagic spots and subsequent ulcers occur in the stomach and colon quite frequently. They are often found at necropsy and are the probable source of the hemorrhages. Lind states that "many at this time are affected with a constant flux accompanied by exquisite pain (possibly a dysenteric-complication), by which they are reduced to the lowest and most weakly condition; while others I have seen without either purging or gripes discharge great quantities of pure blood by the anus."

Effusions of bloody fluid into the pleural or pericardial cavities are not uncommon. Such accidents are followed by pain, dyspnea, oppression and the usual physical signs of fluid in these cavities. Ascites may also occur.

Fever is no part of the clinical picture of scurvy and is not present except when due to intercurrent infections or complications. The heart and circulation become progressively weaker. The patients complain bitterly of dyspnea and oppression of the chest, which may be due partly to the condition of the ribs and partly to blood effused into the chest wall or to pleural effusions. Pain is apt to be constant, the location varying according to circumstance. Even to the last such patients may have a remarkably good appetite considering the condition of the mouth. They retain consciousness with a clear mind to the end, though sometimes indifferent, and often suffering from great mental depression, melancholy and despondency which can hardly be surprising.

Death may be due to a sudden dropsical effusion, to pulmonary edema, to a sudden fatal hemorrhage, or to some intercurrent infection. In advanced stages of the disease sudden death may occur following any unusual exertion. Thus patients who have attempted to go ashore have died while in the boat. "This happened to one of our men when in the boat going to be landed at Plymouth Hospital. It was remarkable he had made shift to get into the boat without any assistance, while many others were obliged to be carried out upon their beds. He panted for about half a minute and then expired." This tendency to sudden death from cardiac failure, as well as the tendency for dropsical effusions in the legs and serous cavities, is very like that part of the clinical picture of beriberi. It might be supposed in such cases that beriberi and scurvy coexisted; but similar effusions into the serous cavities have been found in guinea pigs that have developed scurvy on a diet that could not possibly have produced beriberi. We must conclude, therefore, that these symptoms are common to both diseases, though they are not so prominent in scurvy as in beriberi.

**SPECIAL SYMPTOMS.—The Blood.**—Anemia is generally present, the blood picture being that of secondary anemia. The red cells in cases of average severity fall between three and four millions, but if the hemorrhages are severe the red cells may sink very low. Three hundred and seventy thousand was recorded in one case, and 557,000 in another. The percentage of hemoglobin falls even below the cell count. The cells vary in size and shape, and nucleated reds are common and are often present in numbers out of all proportion to the anemia. Normoblasts are chiefly found, but microblasts and megaloblasts are also common. The leukocyte count may be normal, but is frequently increased, and counts from 20,000 to 50,000 have been recorded. No differential counts have been found in the literature, but counts made on experimental animals show that the polymorphonuclears are decreased and that there is a great increase in the number of large lymphocytes. The very considerable number of these large cells, which may be of endothelial origin, is of considerable significance and may be an evidence of the injury to the walls of the capillaries that undoubtedly occurs.

The blood as it flows appears watery. The coagulation time has been reported to be sometimes longer than normal, but in animals the writer has found it shorter than normal, seldom longer than one minute. When the clot forms it is very firm and dense. Analyses indicate that with the loss of cells there is an increase in the amount of fibrin, albumin and inorganic salts in the serum.

**The Capillary Resistance Test.**—Dr. Hess has devised this test, which is carried out as follows: The arm band of a blood pressure instrument is placed about the arm and inflated until the pressure reaches about 90, or until the venous circulation is just shut off. The pressure is maintained at this level for three minutes and the band is then removed. When the blueness has faded from the forearm and hand, an examination is made for petechial spots. If present, this indicates an increased permeability of the capillary walls, for in the test a mod-

erate excess pressure is put on the capillaries by shutting off the venous but not the arterial circulation. The test is useful both as an additional aid in the diagnosis of scurvy and as an indication of the probability that the hemorrhages, which are so common in scurvy, are probably due to an increased permeability of the capillary walls.

*Nyctalopia.*—The occurrence of night blindness among the victims of scurvy was noticed by Gilbert Blane<sup>7</sup> and others. In an epidemic described by Coale, of 450 men composing the crew, so many were unable to see after sundown that the deck work could not be carried out at night. However, as night blindness may occur in the absence of scurvy, nyctalopia is believed to be a concomitant condition rather than a symptom of scurvy, although its debilitating character undoubtedly serves as a predisposing factor.

**Diagnosis.**—It might be supposed that the clinical complex of scurvy would be readily recognized, but experience indicates that the reverse is the case, especially since scurvy has become comparatively rare and physicians are not expecting to encounter it. The early changes in the gums have been mistaken for pyorrhea. The stiffness in the joints and limbs has been taken for rheumatism, and the subcutaneous hemorrhages may be mistaken for certain forms of purpura. Thus in many outbreaks of scurvy several weeks have passed before the true nature of the disease has been recognized.

The tumefaction of the gums that occurs in scurvy is quite different from the retraction that is seen in pyorrhea, and there is no pus produced in scurvy. Moreover, pyorrhea is a chronic and long-standing condition and does not occur suddenly. Whenever the gums are swollen and bleed easily and the teeth become loose the possibility of scurvy should be considered. An investigation of the diet will soon indicate if scurvy be possible, and the rapid improvement that follows when the deficiency is corrected promptly settles the diagnosis.

No dietary deficiency can be detected in purpura. *Purpura rheumatica* (Schönlein's disease) is characterized by fever, and the purpura is associated with urticarial wheals. Acute articular rheumatism is characterized by fever, sweats and other constitutional symptoms that indicate the infectious origin of the disease; chronic muscular rheumatism is not associated with any swelling or discoloration of the parts such as occurs in scurvy, and rheumatism commonly affects the muscles of the back and trunk rather than the legs.

**Association with Other Diseases.**—Scurvy has often been associated with beriberi, particularly on shipboard, so that the symptoms of the two diseases have been so intermingled as to cause the most hopeless confusion in diagnosis. Since beriberi is another deficiency disease, it is easy to see that if the two deficiencies coexist, both diseases will develop, and the clinical picture will depend upon the preponderance of scurvy or beriberi symptoms.

Scurvy has also been often complicated by infectious diseases such as dysentery, malaria and typhoid fever. Persons suffering from scurvy are, by their debilitated condition, rendered peculiarly susceptible to

infections; while on the other hand, it has often been observed that those weakened by previous infections fell easy victims to scurvy. Indeed, in some of the diseases, particularly dysentery and typhoid, the diet adopted in the treatment was admirably adapted for the production of scurvy, so that the patient suffering from disease became more liable to scurvy than his healthy mates on a full diet. From the nature of the disease scurvy may occur as a concomitant of any infectious or constitutional disease.

**Pathology.**—Information with regard to the pathology of human scurvy is necessarily incomplete. In former times when the disease was frequent and the mortality high, few necropsies were performed and the descriptions of these were often vague and couched in an obsolete terminology. Since the development of pathology as a science, scurvy has been rare. Yet from the descriptions of the older writers, together with the findings in experimental animals, the following picture may be drawn.

**GROSS PATHOLOGY.**—(1) Hemorrhages into the tissues are found as described under the symptomatology. The skin shows the ecchymoses that were present during life. Hemorrhages into the muscles of the legs are very common, and subperiosteal hemorrhages may be found. Lind says, "The quantity of this effused stagnating blood was sometimes amazing: we have opened bodies in which about a fourth part of this vital fluid had escaped from its vessels and in the legs and thighs, the bellies of the muscles seemed generally, as it were, stuffed with it." Effusions and ecchymoses also occur into the internal organs, especially under the serous membranes, and are particularly common on the walls of the stomach and colon, where they appear as extensive bright red patches. The blood-vessels appear normal and are never ruptured, and these effusions of blood must pass through the walls of the capillaries.

(2) Effusions are frequently found in the serous cavities. The liquid is usually red and blood tinged, but may be clear yellow serum resembling the effusions found in beriberi. Pleural effusions are most common, but an increased amount of peritoneal fluid is also often found.

(3) The bones are found to be soft, friable and easily broken. The bones most often and most severely affected are the tibia and femur, ribs and lower jaw, but other bones may be similarly involved. The epiphyseal extremities are more prone to become affected than the shaft, and the epiphyses may become separated either spontaneously or by the exertion of surprisingly little force. Spontaneous fractures of the long bones, and separation of the ribs from the costochondral junction have been found. If the long bones are split open, it will be found that the yellow marrow has entirely disappeared from the shafts and has been replaced by the red marrow normally found in the cancellated bone at the epiphyseal extremities.

(4) The blood is thin and obviously anemic, but coagulation is good, and the blood in the tissues has coagulated firmly so that the limbs possess a brawny appearance. No characteristic changes are found in other organs.

**MICROSCOPIC ANATOMY.**—Parenchymatous changes are frequent in most of the internal organs often associated with congestion and extravasations of blood. Such changes may be found in the liver, heart, kidneys and suprarenal capsules. Stained smears of the blood show a large number of nucleated red blood-cells, mostly normoblasts, but including also some microblasts and megaloblasts. Similar changes may be found in any secondary anemia, but the number of nucleated cells is out of all proportion to the anemia, as indicated by the red cell-count, and this flood of nucleated cells in the circulation is evidently closely connected with the hyperplastic condition of the bone marrow.

Sections through the shaft of the affected bones show that an absorption of the compact bone has occurred. The condition is not a simple decalcification of the bone, for the cartilaginous matrix is bored out and channeled, giving the bone the appearance of a worm-eaten log. This absorptive process is still more marked toward the epiphyses, where it has proceeded until only a spongy network of bony spicules remains. The bone along the line of junction between the epiphysis and diaphysis is completely absorbed, giving rise to what is known as the "white line," and which results in the common separation of the epiphyses.

Sections through the marrow of the shaft show that the fat has entirely disappeared, and that the marrow is markedly hyperplastic. Instead of the normal, spongy network of fibers with a few cells in the interstices, the network is packed so full of cells that it is obliterated from view, and the marrow seems to consist of a dense mass of cells without particular structure. The cellular elements are those found normally in the red marrow of the epiphyses. Multinucleated megakaryocytes are common. This change in the marrow is connected with the anemia, either as cause or effect.

**Treatment.**—**PROPHYLAXIS.**—From the foregoing discussion it is evident that a diet that includes **fresh vegetables or fruits** will prevent the development of scurvy. Scurvy has become a rare disease among adults in recent years, and this is no doubt entirely due to the fact that with the development of cold storage facilities and better methods of transportation, both fresh vegetables and fresh fruits are constantly available throughout the year. On the other hand, the incidence of infantile scurvy appears on the increase *because of the wide use of pasteurized milk.*

The diet of sailors has also been greatly improved. Long voyages are the exception rather than the rule; fresh vegetables and fruits may be carried in cold storage or obtained frequently at the stops in port, and canned vegetables and fruits are often supplied. It has been found that *canned cabbage* and *canned tomatoes* still retain at least a part of their antiscorbutic properties, and this may be true of some other canned vegetables and fruits, though it is certainly not true of all. It has been found that *bottled lime juice* which has been subjected to heat is quite inefficient in preventing scurvy and *should never be used.* The juice with which the British Navy was supplied and protected was **lemon juice** preserved by the addition of one part of strong

brandy to ten parts of the juice. A fluid ounce was served daily to each of the men with an ounce and a half of sugar, and when preserved in this manner the antiscorbutic properties of the juice were unimpaired.

Although the means of preventing scurvy have been well understood for at least one hundred years, we are in considerable danger of forgetting the lessons of the past. Scurvy has been such a rarity for some years that the new generation of physicians do not recognize the disease, and many of them are unaware of the consequences of a monotonous diet of bread, dried vegetables and dried or salted meats. Consequently, we occasionally find scurvy appearing in jails, almshouses, and asylums, or as it did among the British troops in Mesopotamia during the present war, when a little forethought in providing an antiscorbutic would have prevented the disease.

In any given case the choice of an antiscorbutic will depend upon the attendant circumstances, and it would be well if we knew accurately the exact amount of antiscorbutic vitamin in the various available vegetables and fruits. Our information is, however, sufficient to prevent the occurrence of scurvy if the available information is applied.

Of the fruits, **oranges** and **lemons** are particularly rich in antiscorbutic substances. **Limes** are antiscorbutic, but only about one-fourth as potent as lemons. **Apples** and **grapes** have been found effective in curing and preventing scurvy on several occasions, and it is probable that most acid fruits are more or less efficacious; but the exact power of such fruits is unknown. The state of the fruit as to maturity may have some influence on its properties; thus on one occasion it was found that **green guavas** protected while ripe guavas had little value.

It requires from three to five cubic centimeters of lemon or orange juice daily to protect the guinea pig with certainty, and experience indicates that adult men require about an ounce daily when on a scurvy-producing diet. Thus the value of these fruit juices is accurately known.

Of the vegetables, **cabbage**, **onions**, **carrots**, **turnips** and **potatoes** are known by experience to be effective. Cabbage is particularly active and I have found that from one to two grams of cabbage daily is sufficient to protect the guinea pig from scurvy. Sauerkraut has been found a useful preventive. **Lettuce**, **cresses**, and many other vegetables are good preventives, though it must be insisted that they be fresh, and their relative value has never been determined.

It has been shown repeatedly that *drying destroys* the antiscorbutic vitamin, and dried vegetables cannot be used to prevent the disease. The antiscorbutic action of vegetables is greatest when they are eaten raw as in salads, but moderate cooking may not entirely impair their value. Prolonged stewing destroys the vitamin, and such vegetables as must be cooked should be boiled rapidly as short a time as possible. The amount of cooking that can be borne appears to depend to some extent upon the reaction, and acid vegetables probably stand cooking better than alkaline. Alkalis rapidly destroy this vitamin, and soda should never be used in cooking.

**Fresh meat and milk** are relatively poor in scurvy vitamin, and there are many instances cited where scurvy has developed in spite of a supply of fresh meat. It seems probable, however, that if fresh meat be eaten in sufficient amount and is not overcooked that this, too, will protect since there are numerous instances where Indians, Eskimos and explorers have lived upon an exclusive diet of meat for long periods without developing scurvy. Recently Stefanson<sup>18</sup> has described cases, in his expedition, in which scurvy was cured by eating frozen decomposed meat. But meat in the amounts usually consumed, and as usually cooked cannot be relied upon, and some fresh vegetable or fruit must be supplied if scurvy is to be prevented with certainty. If this be impossible, orange or lemon juice must be used as an antiscorbutic. This should be fresh or preserved with alcohol.

If none of these things can be done, then scurvy can still be prevented by **germinating seeds**. It is a noteworthy fact that beans, peas and lentils when dried have no antiscorbutic properties. If, however, the dried seeds are soaked in water and are allowed to germinate for several days, they develop the antiscorbutic vitamin. The method adopted for germination is as follows: the beans or peas are soaked in water at room temperature for 24 hours. The water is then drained away and the soaked seeds are spread out in layers not exceeding two or three inches in depth. They are kept moist for about 48 hours at room temperature (60° F.). After germination they should not be allowed to dry, but should be cooked as rapidly as possible (lentils 20 minutes, peas and beans 40-60 minutes).

**MEDICINAL TREATMENT.**—Kramer's dictum is just as true to-day as when written in 1730: "Scurvy is the most loathsome disease in nature; for there is no cure for it in your medicine chest; no, nor in the best-furnished apothecary's shop. Pharmacy gives no relief, surgery as little. Beware of bleeding: shun mercury as a poison: you may rub the gums, you may grease the rigid tendons in the hams, to little purpose. But if you can get green vegetables: if you can prepare sufficient quantity of fresh, noble, antiscorbutic juices: if you have oranges, lemons or citrons or their pulp and juice preserved with sugar in casks so that you can make lemonade, or rather give to the quantity of three or four ounces of their juice in whey, you will, without other assistance, cure this dreadful evil."

Medicinal treatment is useless except for certain symptomatic purposes. Constipation may be relieved, though care should be used to **avoid purgatives and calomel**. The pains and sleeplessness may be relieved by **morphin**, but this is plainly undesirable for anything than the most temporary use. The same may be said of other symptomatic remedies. Nothing is of avail for permanent relief except the addition of fresh vegetables or fruits to the diet. When this is done the results are miraculous. In the course of a few days the complexion becomes a normal hue, the gums become firm and healthy, the tendency to hemorrhage ceases and the livid spots on the skin disappear. The legs, if

swollen and stiff, regain their normal contour and function, and the patient rapidly regains his former state of health.

(GENERAL MANAGEMENT.—In spite of these extraordinary results it must not be supposed that the patient returns so rapidly to normal. There have been many instances where sailors incapacitated by scurvy have been put ashore for treatment, have recovered in the manner described, and have returned to duty apparently completely cured in a marvelously short time. But when they returned to the original deficient diet aboard ship again, they developed scurvy very quickly. In some cases, this has only been a matter of several weeks, while the depletion period of a normal person is known to be from four to seven months. This indicates that in the short period devoted to the cure of these men, the deficiency from which they suffered was not entirely made up, even though no clinical signs of the disease could be detected.

When the condition of the gums is such as to prevent mastication, the cure may be effected by fruit juices or scraped raw vegetables, the diet in the meantime being restricted to **milk and soups**. Fresh raw milk is itself antiscorbutic when consumed in sufficient quantity. It cannot be relied upon alone for a cure, as milk is relatively poor in scurvy vitamin. Thus from three to five cubic centimeters daily of lemon juice suffice to prevent the development of scurvy in the guinea pig, whereas from 25 to 50 cubic centimeters of milk are required to accomplish the same result. Later the patient should receive a **mixed diet** with an abundance of fresh vegetables and fruit, and it is especially recommended that as far as possible the vegetables should be raw in the form of salads.

The tendency to sudden death on slight exertion in advanced cases has already been noted. Such cases should be **kept in bed** until the cure is well advanced, and should not even be allowed to sit up until sufficient strength has been recovered and all danger of cardiac failure is past.

Any **clean surgical dressing** may be used for the ulcers. No local treatment will have any effect until systemic results have been attained as the result of the necessary additions to the diet, and after these additions the ulcers heal promptly. These ulcers do not resemble syphilitic ulcers, and the other scorbutic symptoms present should indicate their cause. Yet a particular injunction **against the use of mercury in any form** is deemed desirable because mercury is practically a poison in this condition. Death from the administration of mercury has been recorded in several instances, one of which seems almost incredible. According to Kramer, 400 of the troops near Belgrade who were suffering from scurvy, "having taken mercury without my advice, the dreadful consequence was they all died in a salivation." In those days mercury, like other drugs, was given in heroic doses; but the advisability of avoiding mercury is clear.

With regard to infants, it is only necessary to point out that milk is rich in antiscorbutic substance. When raw milk is used, it will probably protect; it will surely protect when the diet consists of milk



alone. But when the bulk of the diet consists of farinaceous foods, or when milk that has been pasteurized or otherwise heated is used, a few teaspoonfuls of orange juice should be given daily to prevent scurvy. Orange juice in larger amounts may also be relied upon as a cure in cases where it has already developed. Hess has found that an extract of the orange peel is quite efficient and this may be used by the poor who are unable to afford the luxury of fresh fruit.

**Prognosis.**—There are great individual variations in susceptibility to the deficiency that causes scurvy. All men or experimental animals do not develop scurvy at precisely the same time, though living on the same diet; and when the disease has developed some die very promptly, while others live a long time, although they have obvious and perhaps severe symptoms of scurvy. Thus in Lord Anson's voyage, practically all the crew had developed scurvy by the first of May, and they did not reach land till the middle of June. During this time more than half the cases on the *Centurion* died, while on the *Gloucester* about three-fourths of the cases died.

We may say, therefore, that when scurvy has developed, the *prognosis as to life* is exceedingly bad unless the diet is changed in accordance with previous directions. On the other hand, when the proper diet has been adopted the prognosis as to life is excellent. Practically none die except those in the last stages of the disease, and even some of these recover.

The *prognosis as to recovery* of function is also favorable. Only in the cases where contractures and partial ankylosis of joints has occurred the prognosis must be more guarded. From what has been said with regard to the pathology of such joints, it will be seen that a return to normal will be slow. When extensive adhesions of the synovial membrane and bony surfaces of the joint have occurred, complete recovery can hardly be expected. Fortunately, such cases are never seen to-day because the scorbutic state is never allowed to exist for a period sufficiently long for such changes in structure to occur.

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## CHAPTER X

### INFANTILE SCURVY

(*Barlow's Disease*)

BY FRANK C. NEFF, M.D.

Definition, p. 179—Etiology, p. 179—Predisposing causes, p. 179—Experimental studies, p. 180—Etiological summary, p. 181—Symptomatology, p. 182—Physical findings, p. 182—Constitutional symptoms, p. 183—Laboratory findings, p. 183—Roentgen-ray findings, p. 184—Diagnosis, p. 185—Association with other diseases, p. 185—Treatment, p. 186—Prognosis, p. 186—Pathology, p. 186—Historical summary, p. 187—Sociological aspects, p. 187—References, p. 188.

**Definition.**—Scurvy in infancy is a nutritional and hemorrhagic disease appearing as early as the third month of life, usually after the sixth month, and finding its most common incidence at the age of ten months. A few cases occur as late as eighteen to twenty-four months. The disease is rarely sudden in onset, but usually requires several months for its development. The impaired appetite and the increasing pallor of an infant fed for long periods on an artificial food of improper nature and sameness is characteristic of the earlier stage. The child has not only digestive disturbances, but has failed to gain in weight and in the size and length of bones. Edema of the eyelids and over the lower end of the tibia is an early symptom.

**Etiology.**—PREDISPOSING CAUSES.—Infantile scurvy, as already stated, seldom develops before the age of six months, and is most often found at an average age of ten months. The writer has seen one case as late as twenty-five months occurring in a child who refused to take any food but malted milk and water. It is improbable that there is any hereditary or familial tendency to the disease, though it is well known that not all infants will develop it on a faulty diet which is identical with that which has caused it in a given case. It has been suggested that the child who has the exudative diathesis is prone to develop the disease, but this is not yet proved. It is found among the well-to-do and the poor, among country and urban children. Nor does bad hygiene or institutional life seem to excite or predispose to it. The early months of life are spared either through an immunity acquired from the mother or because the disease requires usually several months before it fully develops.

The absence of the so-called antiscorbutic element in the dietary of those who develop the disease and their prompt cure by the inclusion of this element in the food shows that in any given case the causative factor is a *dietary* one.

Many of the experiments dealing with the causation and cure of scurvy have been upon laboratory animals, especially the guinea pig. It is not yet proven that the animal disease is identical with the human scurvy. A diet of rolled oats and fresh milk will cause the disease in from three to four weeks in the guinea pig, while the same diet may permit of scurvy in infants but seldom does. The same antiscorbutic element will, however, cure it in both species.

For years it has been known that cases of scurvy had been fed on canned and proprietary foods, that the disease developed on a dietary of boiled or pasteurized milk, and we have seen cases arising in the infant fed on raw milk; it has also occurred in breast babies, though rarely.\* But a small percentage of the babies fed on these foods develop scurvy. So there must be some unsuitability peculiar to the individual child which permits of the disease developing. The best explanation yet given is that of food aging. Canned foods are old; most pasteurized and boiled milks in urban communities are old by the time they are used. Heating milk kills the lactic organisms and retards or prevents souring with the resultant formation of putrefactive microorganisms in the milk. Such milk is unsuited to the infant's digestion and can easily so change the intestinal flora as to be incompatible with health. Experiments on the therapeutic value of antiscorbutics in the disease show that desiccation or aging usually affects their potency. Also the small amount of antiscorbutic substance that a food such as cow's milk contains may be still further reduced by dilution in the infant's formula until it is insufficient for individual needs.

EXPERIMENTAL STUDIES.—Any consideration of the etiology of scurvy must recognize the many interesting though somewhat conflicting opinions regarding the causative factors which have been suggested in the last few years. Funk's hypothesis of a deficiency of the accessory food substances which he calls vitamins has been offered as an explanation. These substances are of unknown chemical nature. Funk believes that nicotonic acid is a decomposition product of the vitamins. Williams found that the polyneuritis of pigeons is cured by crystalline forms of certain substances, especially a hydroxy-pyridin.

McCollum<sup>2</sup> does not believe that the existence of a specific substance has been proven. Two chemically unidentified substances must be present in a healthful diet. He has designated these "fat-soluble A" and "water-soluble B." The absence of the former in the diet of an animal causes a peculiar eye affection, xerophthalmia; the absence of the latter causes polyneuritis or beriberi. He thinks these are the only

\* An interesting light is thrown upon the types of foods in a summary of 50 cases studied by McLean<sup>1</sup> (*Arch. Pediat.*, August, 1918, xxxv, 447):

22 per cent. of the infants were fed on proprietary foods alone.  
 22 per cent. on boiled milk with proprietary food.  
 6 per cent. on condensed milk alone.  
 8 per cent. on breast milk alone.  
 4 per cent. on breast milk and a proprietary food.  
 23 per cent. on pasteurized milk alone.  
 12 per cent. on pasteurized milk with a proprietary food.

true deficiency diseases. Scurvy is due to faulty diet, but can be explained by the staleness of pasteurized milk, for instance, which is not bacteriologically in good condition, due to putrefactive forms of bacteria which develop in it. These change the character of the feces, with resulting injury to the bowel wall and subsequent infection. He has cured experimental scurvy in guinea pigs with mineral oil as a laxative. A diet which causes the feces to be promptly evacuated will relieve or prevent scurvy.

Hess<sup>3</sup> believes that the faulty diet of scurvy permits the presence of harmful bacteria in the intestine and the formation of bacterial toxins which play a part in the development of scurvy.

Jackson<sup>4</sup> found diplococci of low virulence in the culture of crushed tissues from guinea pigs suffering from experimental scurvy. The microorganisms were found in the region of the osseous-cartilaginous junction in an active process characterized by cell degeneration, and fibrin formation invading the blood-vessel and accompanied by hemorrhage. However, these cocci may be only secondary invaders.

Pitz<sup>5</sup> states that, in experimental scurvy in guinea pigs, the combination of calcium and chlorin in the form of calcium chlorid protects the animal. He thinks the physical character of the diet and the intestinal bacteria are important in producing the disease. Calcium salts in a complete diet control the permeability of the tissues. Retention of the feces is a factor by reducing peristalsis and the intestinal secretions, causing intestinal lesions, weakening the blood-vessel walls and thereby aiding in the absorption of toxins.

There is no question that orange juice possesses the antiscorbutic principle. To what it owes this is not yet proven. It is not probable that the small amount which is sufficient to cause immediate improvement in scurvy can cause any laxative effect in the child. Experiments by Harden and Zilva<sup>6</sup> show that orange juice made alkaline by the addition of sodium hydrate loses its antiscorbutic property, which evidently is inherent in the acidity or moderate neutrality of the orange juice.

These same experimenters working with Still<sup>7</sup> found that after the removal of the free citric and other acids from lemon juice the residue contains the entire antiscorbutic activity. They have found this residue concentrated to small bulk potent, convenient, and readily tolerated in the treatment of infantile scurvy. It cures the disease more readily than does the orange juice. Such a preparation, if it retain its properties after aging, will prove of economic and therapeutic benefit.

Chick and Rhodes<sup>8</sup> found that next to orange juice, the raw juice of rutabaga is the most potent. It has recently been adopted in some infant welfare centers. Dosage in infants is not given, but it protected guinea pigs in doses of 2.5 c.c. daily.

Numerous workers<sup>9</sup> have testified to the value of raw fresh tomatoes, and those dried at a high temperature are still sufficiently potent, one gram of the dried tomato being sufficient for a guinea pig. An infant could require one-half to one teaspoonful of the powder.

ETIOLOGICAL SUMMARY.—Scurvy is due to a diet unsuited to the in-

dividual child. Too long an administration of a single food, sameness of diet, the use of canned or dried milk, or of old milk, whether pasteurized, boiled or raw or of too greatly diluted milk, the absence of essential healthful elements in the food, the presence of harmful putrefactive bacteria—one or more of these conditions are responsible for the disease as it is found in infancy.

**Symptomatology.**—**PHYSICAL FINDINGS.**—Perhaps the manifestation which first gives warning that the infant is in a serious condition is the marked tenderness displayed by the child on being handled, the legs no longer being moved. When to these signs is added the appearance of purplish hemorrhagic gums, ecchymoses and petechiæ of the skin, a syndrome is present which should be recognizable by the physician who has had any experience in the study of infancy.

The findings in detail which are most common and which will render the observer familiar with the clinical picture are:

**Hemorrhage.**—Scurvy usually makes its appearance at the age in which the eruption of teeth is occurring: the gums will be found to be markedly inflamed, purplish, and bleeding occurs from the injured mucous membrane. In half of the cases where teeth have not yet appeared, hemorrhagic gums will be found.

**Ecchymosis.**—Ecchymosis of the orbit with resulting prominence of the eyeball is present in some cases. Petechiæ of the skin and ecchymoses of the superficial areas are often observed. Hematomata have been occasionally found.

In some cases there are hemorrhages from the bowels, the mouth, and other mucous surfaces. Hematuria is a frequent symptom. The essential hemorrhage is subperiosteal and will be described under the *x-ray* and pathological findings.

**Tenderness.**—On being handled, the infant displays evidence of pain in the back and in the extremities. The child is fretful, fears approach, and in self-protection holds his body absolutely quiet. Abeyance of motion amounts to a pseudo-paralysis, but the reflexes are markedly present. The infant no longer attempts to crawl or to walk. The legs are involved much more often than the arms, the latter always in association with the legs. In 400 cases reported by O'Shea, the arms were involved in only twenty.

**Swelling.**—This manifestation in infants is seldom found in the muscles; it is usually fusiform in outline and occurs along the shaft or near the epiphysis of the bone, usually of the legs, but occasionally in various other locations, even over the flat bones and the skull. The swelling is painful to the touch, and is due to distention from hemorrhage.

**Attitude.**—The position of the patient is characteristic, at least in the advanced cases: the legs and the thighs are partially flexed, with outward rotation of the hips.

**Pallor.**—The marked cachexia is evidenced by the paleness of the skin, and secondary anemia advances with the disease. In the child whose picture is herein presented, the pallor resembled that of a lymphatic leukemia.

*Edema.*—The eyelids and the soft parts overlying the long bones, especially the tibia, are edematous. This may be present either in early or advanced cases.

*CONSTITUTIONAL SYMPTOMS.*—A certain degree of *fever* may be present, usually not above  $101^{\circ}$  F. ( $38.3^{\circ}$  C.). The child appears sick and cachectic. There are *digestive disturbances* in probably half of the cases, mild intestinal intoxication with or without constipation. The failure to gain in weight and the lack of general development shows that the disease is a nutritional one in which the vessels share.

Subsequent studies of scurvy will throw light upon some other symptoms, recently reported,<sup>10</sup> in which a similarity to infantile beriberi and other dietary diseases has been noted. *Cardiac hypertrophy and dilatation, neurological manifestations*, such as increased patellar reflexes and edema of the optic disks have been found in certain cases of scurvy.



FIG. 1.—CHARACTERISTIC ATTITUDE IN SCURVY.

*LABORATORY FINDINGS.—Blood.*—No evidence of disturbance in the clotting time or coagulability of the blood has been discovered. The hemorrhagic tendency depends mechanically upon the lessened vessel-wall resistance with its increased permeability. By traumatizing the areas overlying the superficial bones, hemorrhages may be produced, and petechiae be made to appear in the skin by the application of a tourniquet to the arm above the elbow. This latter phenomenon has been noticed in infectious diseases, and described in scarlet fever as the Rumpel-Leede sign and in scurvy as the “capillary resistance test” of Hess. Tissue section has not as yet demonstrated the minute pathology of the blood-vessel wall in infantile scurvy.

The blood picture is that of a secondary anemia. A typically advanced case recently seen by the writer had a hemoglobin percentage of 55, and a red cell-count of 1,880,000. There is nothing peculiar to scurvy in the differential count. There is no reduction in the calcium or phosphorus content of the blood, except possibly in the period of convalescence when there is decreased calcium retention.\*

\* According to the work of Hess and Killian,<sup>11</sup> reported late in 1918, infantile scurvy uncomplicated by tetany or rickets, showed in five cases a marked blood cal-



*Urine.*—The urine shows a markedly reduced excretion. Hematuria is present in many of the cases. These conditions are sometimes overlooked because of the failure to examine the urine of infants.

*Feces.*—Hemorrhagic stools are sometimes observed.

**ROENTGEN-RAY FINDINGS.**—Several years ago the presence of the "white line" in the roentgenograms of scorbutic bones was noticed. This line is seen at the epiphyseal-diaphyseal junction, is uniformly pres-



FIG. 2.—THICKENING OF CORTEX OF HUMERUS FROM SUBPERIOSTEAL HEMORRHAGE IN INFANTILE SCURVY.

ent. It is found early in the disease, and is due to the greater density of that portion of the bone. Its correct interpretation is a diagnostic sign of value.

The picture of the long bones shows characteristic thickening of the cortical shadow, which is due to the stripping of the periosteum and extravasation of blood beneath it, frequently the entire length of the bone. Periosteal stripping is said to occur more readily in infants than

in adults. In the case of infants, the content being much below the normal of 10 mg. to the 100 c. of blood. The same workers reported also a moderate acidosis, but this is not striking.

adults. Where this has been localized and the hemorrhage abundant, the shadow is obviously wider. This abnormal shadow is due to hemorrhage and not to an epiphysitis.

Separation of the epiphysis sometimes occurs in the long bones.

Fracture of the bones has been reported.<sup>12</sup>

**Diagnosis.**—The picture of scurvy which is diagnostically complete shows an infant, usually above the age of six months, artificially fed, and upon a stale, incomplete and unvaried diet, developing a loss of appetite, a cachexia, a pallor, secondary anemia, tenderness of the back and limbs, disability, swelling and edema of the extremities and eyelids, exophthalmos, characteristic attitude of the legs, hemorrhage of the gums

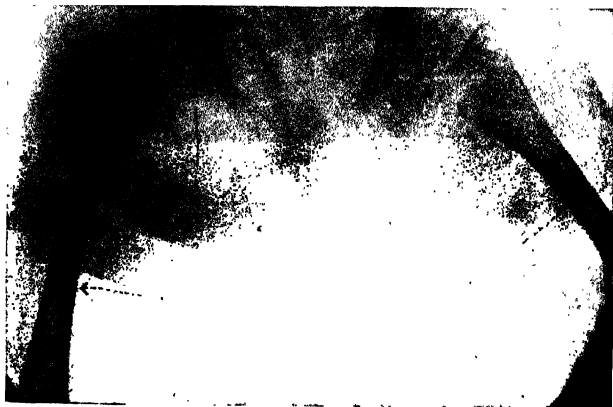


FIG. 3.—THICKENING OF CORTICAL SHADOW OF FEMUR FROM SUBPERIOSTEAL HEMORRHAGE IN INFANTILE SCURVY.

and skin, scanty and hemorrhagic urine, and the *x-ray* findings of a white epiphyseal line and of subperiosteal hemorrhage.

The characteristic symptoms of *rickets* are missing, with the exception of disability. Parrot's paralysis of infantile syphilis occurs at the earlier age of about six weeks. *Infantile paralysis* is easily differentiated by the marked clinical difference.\*

**Association of Scurvy with Other Diseases.**—There have been many efforts to establish the identity of scorbutus and rachitis. The hemorrhagic nature of scurvy and its specific dietary curability prove that it is a disease apart from rickets. That the same infant may acquire rickets, which is the most common disease of infancy, is not unlikely.†

Similar bacterial involvement of the bones in scurvy and rickets have been reported, but these were probably accidental and not causative

\* Comby<sup>13</sup> reports 55 cases of scurvy of which 45 had been diagnosed as acute myelitis, syphilis, acute osteomyelitis or rheumatism.

† Morse<sup>14</sup> reported rickets present in all but 9 of 50 cases of scurvy.

factors. A few cases of cure of rickets by the administration of orange juice have been reported. Both diseases have been by some writers included in the list of deficiency diseases.

Hereditary lues, tuberculosis, and various nutritional diseases may sometimes coexist with scurvy, but this cannot be regarded other than as accidental.

**Treatment.**—The present tendency is to reduce the age at which a small amount of antiscorbutic diet is begun from the customary six months to as early as one month. In case the infant is getting entire or part breast food other antiscorbutic diet at this period is unnecessary. Of importance, then, is the maintenance of some **breast feeding** to the ninth month. When infants are wholly artificially fed and show any nutritional disturbance it should be the common practice to **broaden the ordinary milk dietary** with the addition daily of an antiscorbutic food. Of more importance is the feeding of **fresh milk** equal in nutritional value to the requirements of the individual child. At six months of age a diet of **soup made from fresh vegetables**, administered once daily, should be carefully begun. To this may be added a **cereal** by way of variety and increased food value. Evidence of smooth digested stools should be the guide for the increases in the milk which will be made from week to week sufficient to meet the needs of a growing infant.

As the disease is essentially due to dietary errors, there should be a change from preserved, stale, or canned foods to milk which has not aged. Milk should not be over 24 or 36 hours old when fed. If the milk is clean and kept iced, it need not be heated until shortly before the time of feeding. It may then be pasteurized or boiled without danger to the child. Insufficient amounts of milk contain a small percentage of whatever antiscorbutic elements that milk contains. A change in the milk formula of the scorbutic child should include a different variety of carbohydrate, especially if a malted food has been previously used.

No results in therapeutic feeding are so spectacular as the improvement accompanying and the cure quickly following the administration of **orange juice**. In this country oranges can practically always be obtained. A teaspoonful to a tablespoonful three times daily is sufficient in the average case of scurvy. An infusion of **grated orange peel** may be equally well used to supplement the supply of orange juice. **Lemon juice, grape juice, scraped apple, potato water or potato cream** are sometimes desirable alternatives. The writer has also occasionally employed a suitable **wet-nurse**.

**Prognosis.**—Few recognized cases have died, the number of reported autopsies being few. Death from asthenia in the untreated or neglected cases and from intercurrent diseases may occur.

The outcome of the treated case is uniformly good for complete recovery. Improvement begins in 24 to 48 hours and the infant is usually well in from one to three weeks.

**Pathology.**—While a uniform and essential hemorrhagic lesion is found underlying the periosteum and in the marrow of the long bones, there is no reason to conclude that this is the origin and point of distri-

tion to the other organs involved. It is nearer correct to regard scorbutic disease as a constitutional one with hemorrhage outbreaks due to the weakened blood-vessel walls. This permits bleeding under the periosteum, into the bone-marrow, into the skin and muscles, from the mucous membranes, from the kidneys, and, in fact, as a survey of the literature will reveal, there are few portions of the body exempt from the possibility of hemorrhage. The increased density of a portion of the bone at the epiphyseal line can be said to be the only definite bone lesion. The separation of the epiphysis which occurs can be explained by the changes resulting from the adjacent hemorrhages. Decreased amounts of calcium and phosphorus in scorbutic bone, as reported by Bahrt,<sup>15</sup> may be due to the coexistence of rachitis, a possibility which is difficult to exclude because of its great frequency and the difficulty of determining mild grades of rickets.

The decreased water excretion from the kidneys in scurvy may be compensated by the transfer of water to the edematous tissues or to the lungs, as suggested by Gerstenberger.<sup>16</sup>

Cardiac hypertrophy, chiefly of the right ventricle, is said by Hess<sup>17</sup> to be a frequent finding in scurvy. Much interesting light is being thrown upon the lesions, symptoms, and etiology by recent investigations. Whether all the manifestations are secondary to the hemorrhagic diathesis, we should not lose sight of the fact that scurvy is a profound disturbance of nutrition and development.

**Historical Summary.**—In 1878 Cheadle, of England, first recognized the identity of infantile and adult scurvy. Sir Thomas Barlow, in 1883, published a complete monograph on infantile scurvy, and the disease has often been known by his name.

In America, Northrup, Holt, Rotch, Morse, Starr, and others were among the first to collect and analyze cases of scurvy. Since then the literature has been full of contributions to the subject. The disease as now known is therefore the study of the past forty years.

**Sociological Aspects.**—The commercial employment of mothers which necessitates weaning the infant, and the economic necessity for feeding canned and inferior grades of milk, are factors in the development of nutritional disturbances in the infant. The establishment of milk stations where proper milk feeding is practiced and where the early manifestations of disease are recognized and corrected will do much to overcome the harmful results of the above-mentioned conditions.

Clean, fresh milk should be within the reach of children of all classes, and for the artificially fed infant, the feeding of a proper dietary should be a matter of common knowledge and attainment. Such an easily prevented disease as scurvy will thereby become a rarity.

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## CHAPTER XI

### BERIBERI

BY EDWARD B. VEDDER, A.M., M.D.

Definition, p. 189—Etiology, p. 189—Symptomatology, p. 193—Differential diagnosis, p. 199—Complications, p. 200—Treatment, p. 201—Prognosis, p. 203.

**Definition.**—Beriberi is a disease resulting from faulty metabolism and is directly caused by the deficiency of a certain accessory food principle or vitamin in the diet. This deficiency is usually produced by the too exclusive use of polished rice, white wheat flour and other carbohydrate staples which are lacking in these necessary vitamins. Clinically beriberi is characterized by degenerative changes in the nervous system including a multiple peripheral neuritis, combined with generalized edema, serous effusions, and a tendency to cardiac derangements followed by sudden cardiac failure.

**Etiology.**—The development of knowledge concerning the etiology of beriberi is one of the most interesting chapters of medicine of which only a bare outline can be given here. The writer has elsewhere discussed this more fully.<sup>a</sup>

Older writers like van Leent correctly attributed beriberi to a monotonous, one-sided and deficient diet. But with the development of the science of bacteriology this view was for a time obscured, and the disease was thought to be infectious. Many investigators found bacteria in the stools, from blood cultures and from the tissues of beriberi patients. But the methods used were crude, the organisms found were as various as the investigators, and in no case were Koch's postulates fulfilled or any real proof afforded that the organisms incriminated really caused beriberi. Later investigations with improved technic have shown that the blood is sterile, and the conception that beriberi is infectious, is utterly discredited to-day.

Other observers have thought that beriberi is due to some intoxication. This view is chiefly due to the clinical resemblance of beriberi to cases of toxic peripheral neuritis. However, all efforts to demonstrate the existence of such a toxin have failed, while on the other hand a great body of evidence has been accumulated which proves that beriberi is directly due to the deficiency of certain substances, the so-called vitamins, in the diet. This view is generally accepted to-day. But just as there are objectors who reason illogically against the efficacy of vaccination as protection against smallpox, so there are objectors to the deficiency vitamins as the cause of beriberi.

It would be impossible within the limits of such an article to discuss all the objections that have been thus urged against the validity of the deficiency theory. The numerous reports of beriberi occurring on a diet that was well balanced and sufficient can in most cases be readily shown to be due to the ignorance of the observer with regard to the numerous foodstuffs that are deficient in antineuritic vitamin, and sometimes to the erroneous supposition that rice is the only deficient food. In several such instances rice has been eliminated from the diet, and wheat flour or another deficient food has been substituted. When beriberi continued on this diet the conclusion has been drawn that beriberi was not of dietetic origin. Again it has been argued that beriberi cannot be due to the deficiency of any particular substance in the diet because starving men or animals do not develop beriberi, and if they receive no food at all they must suffer from the supposed deficiency. But no man can live without food for three months which is the depletion period for beriberi, and death from starvation occurs before the time for the appearance of the symptoms of beriberi. Even in the case of the fowl, which has the shortest depletion period of any known experimental animal, it has been found that these birds die of starvation before they develop symptoms of polyneuritis. However, if the nerves of fowls that have been starved are examined, degeneration of these nerves will be found, indicating that they have suffered from the deficiency of antineuritic vitamin, and would have developed symptoms of polyneuritis had they lived long enough.

Certain investigators, however, still hold that as the result of the dietary deficiency which is admitted, an intoxication develops in the body which produces the degeneration of the nervous system and the consequent symptomatology of beriberi. The writer does not hold this view, but rather that all the tissue changes are directly or indirectly the result of a disturbance of anabolism caused by the deficiency of substances vitally necessary for the upbuilding of those tissues. The vitamins are actually present in most of the bodily tissues, and appear to be in largest amount in those tissues such as the nervous system and heart muscle, which show the most extensive degeneration when the vitamin is deficient. There are also observations that indicate that of two groups of men on the same diet, as sailors and stokers on the same ship, the beriberi may be confined to the stokers or those who perform excessive labor. Yet it must be admitted that this is speculation and that at present there is insufficient evidence to indicate the exact physiological action of the vitamins.

The evidence which proves that beriberi is due to the deficiency of vitally essential constituents of the diet, or vitamins, may be summarized as follows:

(1) EPIDEMIOLOGICAL.—The observations of a large number of investigators in widely separated countries have established the fact that beriberi appears when decorticated rice—rice from which the external layers have been completely removed—is used as the main staple of diet for any length of time. Also that these outbreaks of beriberi disappear when

whole or undermilled rice is substituted; and that beriberi never appears when undermilled rice only is used. Undermilled rice has most of the external layers intact as indicated by examination or by a phosphorus pentoxid content of at least 0.4 per cent. The following illustrations are typical. Vorderman analyzed the statistics from 279,623 prisoners from the prisons of Java and found that of 51 prisons in which decorticated rice was eaten, beriberi developed in the proportion of one case to each 39 prisoners; while in 37 prisons using undermilled rice as the staple food, beriberi only occurred in the proportion of one case to 10,000 prisoners. Undermilled rice was then generally adopted and beriberi was eliminated from these prisons.

Braddon pointed out that beriberi was unknown among the Tamils, a race living in the Malay States, although other inhabitants of the Malay States suffered severely. These races differed only in their dietary habits, the Tamils eating cured or parboiled rice, while the other races ate the ordinary decorticated rice. Cured rice is parboiled before husking, and as a result of this treatment the husk is easily removed, leaving the external layers of the grain intact.

In a similar way, beriberi has been completely eradicated from the Philippine Scouts. This is a body of native troops approximately 5,000 strong. For many years they were supplied with decorticated rice and they often had as many as five hundred cases of beriberi annually. Undermilled rice was substituted in 1910. During this year there were only about 50 cases, in 1911 there were two cases, and in 1912 three cases. These scattered cases were found to occur among men who had not eaten the undermilled rice. Undermilled rice has continued to be used, and beriberi has remained absent. A similar improvement has been made in all civil institutions in the Philippines which are furnished only undermilled rice.

(2) THE HUMAN FEEDING EXPERIMENT OF FRASER AND STANTON.—These observers took 300 Javanese laborers into a virgin jungle where they were employed on construction work, and divided them into two groups. The first group was fed decorticated rice and the second group was fed cured rice which is a whole rice. In three months beriberi appeared among the group of laborers eating decorticated rice, but it did not appear among the laborers eating the whole rice. The conditions were then reversed. The group which had received cured rice was given decorticated rice, and after a somewhat longer depletion period beriberi appeared. The experiment was well controlled, and the patients and the diets were often changed about, but the beriberi always followed the introduction of the decorticated rice, and did not appear when whole rice was used. A somewhat similar experiment with similar results was subsequently performed by Strong and Crowell in Bilibid prison in Manila.

(3) ANIMAL EXPERIMENTS.—Eijkman found in 1890 that fowls fed on decorticated rice developed a paralytic condition similar to beriberi which has been called polyneuritis gallinarum. Fowls fed on whole rice or decorticated rice plus the rice polishing removed from the rice



in the milling process, were always protected. It became evident that the rice polishings contained some substance which protected the fowl from the development of polyneuritis, just as the same rice polishings protected man from beriberi.

Numerous observers attempted to identify this substance, and it was soon found that it could be extracted from the rice polishings by water and by alcohol, but not by ether; that it was dialyzable, was destroyed by heating to 120° C. (248° F.), and that it was adsorbed from extracts by animal charcoal or kaolin. These physical characteristics indicated that the protective substance could not be an albumin, a fat, a lipoid, or an inorganic salt. It was then shown that it could be precipitated from the extract of rice polishings by phosphotungstic acid. This precipitate was broken up by barium hydroxid, the filtrate neutralized and precipitated with silver nitrate. Purin bases are precipitated by this method and were found inactive. The filtrate was rendered alkaline and again precipitated by silver nitrate. This precipitates the pyrimidin bases and this precipitate was found to be active. From it crystalline substances were obtained which in doses of a few milligrams would promptly cure fowls that had developed polyneuritis as the result of feeding exclusively upon decorticated rice. This is the substance to which Funk gave the name of vitamin. It has never been obtained in a chemically pure state, and has not been identified, but from its reactions it apparently belongs in the pyrimidin group. It contains no phosphorus. The difficulty in obtaining it in a pure state is mechanical, for the substance is very fragile and is decomposed and lost in large part during the chemical manipulations. Thus but a few milligrams of crystalline vitamin may be obtained from several hundred pounds of polishings, and even this is lost in the purifying process. The isolation of pure vitamin therefore depends upon the discovery of a chemical process in which this destruction will not occur. Other observations indicate that the substance is capable of forming isomers which have lost the curative property possessed in the original form.

Three pyrimidins are known, thymin, cystosin and uracil, but it does not appear that the antineuritic vitamin is either of these bases, but more probably a new and hitherto unidentified base of this group. The pyrimidin bases are known to be constituents of nucleic acid.

But though none of the vitamins have been isolated and identified, the fact that the antineuritic vitamin exists and will cure and prevent polyneuritis among fowls fed on diets that produce this condition, has been definitely established. There can be little doubt that the deficiency of this same substance produces beriberi in man. The exact chemical constitution of the vitamins, the mode in which they are utilized in the body, and the relation of the antineuritic vitamin to the antiscorbutic vitamin remain as most interesting and important problems for future work.

Later experience with men and feeding experiments with fowls have shown that a number of foods, in addition to decorticated rice, will produce beriberi in man and polyneuritis in birds. Such foods include

other grains that have been decorticated in the milling process such as wheat and corn. Bread made from fine wheat or corn flour, biscuit, macaroni, corn meal, hominy, corn starch and similar products made from wheat and corn; other carbohydrate foods such as sugars, molasses and honey; the hydrocarbon foods including the various animal and vegetable fats and oils, are all beriberi producers. Potatoes and yams, at least as ordinarily cooked, also belong in this group.

It has also been found that although the antineuritic vitamin, as it occurs in food, withstands boiling temperature, it is destroyed by sterilization. It follows therefore that the vitamins are destroyed in many canned foods including meats and vegetables containing much proteid. Such foods must be subjected to temperatures above 100° C. (212° F.) in order to sterilize them. Practical experience on ships and with laborers and troops supplied with canned goods has demonstrated that canned meats, peas and beans cannot be relied upon to prevent beriberi, and polyneuritis has been produced in fowls by feeding canned foods.

It is largely due to the failure to recognize these facts that discredit has been cast upon vitamin deficiency as the cause of beriberi. It will be readily seen that a diet can easily be selected from the deficient articles named above, which will provide a sufficient number of calories and be well balanced in the proportion of proteid, fat, carbohydrate and mineral salts, and yet be very deficient in antineuritic vitamin. It must also be recognized that in institutions such as prisons and asylums there may be some individuals who will fail to eat the whole ration and will select deficient foods so that cases of beriberi may appear although the ration appears to provide against this contingency.

In addition to the external layers of the various grains it has also been found that barley, yeast, and the numerous varieties of peas and beans are very rich in antineuritic vitamin and will prevent beriberi if consumed in moderate quantity. Milk, meat and eggs contain antineuritic vitamin but in relatively small amount, so that considerable quantities of these foods must be consumed to secure protection when living on staples that are known to be deficient.

**Symptomatology.**—THE DEPLETION PERIOD.—Pathological changes in the nervous system can be demonstrated shortly after the adoption of the faulty diet, so that the physical impairment as the result of the faulty diet begins at once; however, this impairment does not lead to symptoms that can be detected, until it has proceeded to a given point. The length of time that will elapse between the adoption of a deficient diet and the first appearance of the symptoms of beriberi has been definitely established by the human feeding experiments of Fraser and Stanton<sup>1</sup> and Strong and Crowell,<sup>2</sup> and from the evidence afforded by certain epidemics. The shortest period recorded is 72 days.<sup>3</sup> In Fraser and Stanton's experiment, the symptoms first appeared after 89 days' feeding. The depletion period can, therefore, be placed with great exactness at from three to four months. As in the case of scurvy it will be longer among resistant and previously well-nourished individuals, and shorter among the susceptible and poorly nourished.

**TYPES OF THE DISEASE.**—The symptoms of beriberi may be divided conveniently into three categories which correspond to the pathological alterations, namely:

- (1) Symptoms attributable to degeneration of the nervous system.
- (2) Generalized edema and serous effusions.
- (3) Changes in the heart muscle often resulting in sudden cardiac failure.

The clinical picture presented by any particular case of beriberi depends upon the manner in which these three types of symptoms are blended together. There are many cases in which the symptoms are chiefly or solely dependent upon the degeneration of the nervous system, and such cases are now regarded as "*dry beriberi*." On the other hand, there are cases in which the symptoms are chiefly or solely those resulting from the generalized edema and serous effusions. Such cases are now called "*wet beriberi*." The tendency to sudden cardiac failure may be found in either of these two main types of the disease, but is perhaps more frequently seen in the wet type.

Some of the older writers, for example, Le Roy de Mericourt,<sup>4</sup> thought that the disease which we here describe as beriberi in reality consisted of two diseases: *barbiens*, corresponding to dry beriberi, and beriberi, corresponding to wet beriberi. But Malcolmson<sup>5</sup> and others showed that these two conditions frequently co-existed, and that, although the disease might begin as wet beriberi, it frequently terminated as dry beriberi and *vice versa*, so that in late years it has been customary to describe dry beriberi and wet beriberi as types of the same disease. It may be pointed out, however, that there is considerable experimental and clinical evidence<sup>6</sup> indicating that there are at least two vitamins that are deficient in beriberi, and that the deficiency of one, generally called the neuritis preventing vitamin, is responsible for the degeneration of the nervous system and the resultant symptoms of dry beriberi; while the deficiency of the other vitamin, hitherto unnamed, results in the production of generalized edema and the symptoms of wet beriberi.

**Infantile Beriberi.**—This is an acute or subacute manifestation of beriberi affecting infants who are nursed by mothers suffering from manifest or latent beriberi. The disease is characterized by cardiac hypertrophy and a peripheral neuritis and results in a clinical picture of generalized edema, dyspnea, palpitation and epigastric pain, gastrointestinal derangements, oliguria and aphonia. Like beriberi in adults, it is caused by the deficiency of vitamins in the food, i.e., in the milk of the mother who is suffering from a similar deficiency. This condition was first described in infants by Hirota in 1888. It has since been found that a large part of the infant mortality in the Philippines is due to infantile beriberi. The symptomatology in infants is necessarily purely objective, but agrees entirely with the objective symptoms in adults. The writer has described infantile beriberi more fully elsewhere.<sup>6</sup>

**THE ONSET AND COURSE.**—The onset of beriberi may be sudden, but is generally insidious, and the so-called acute pernicious or fulminating beriberi is generally an acute exacerbation in a patient who has suffered

for some time with mild and possibly unnoticed symptoms of the disease. Usually, for several days or weeks, the patient experiences a heaviness of the legs and increasing inability and indisposition to walk. The calves of the legs are the muscles most commonly affected first, and these muscles feel stiff and are often painful when squeezed. There may also be some loss of cutaneous sensation over certain areas, particularly over the tibiae. Combined with these symptoms, slight edematous swelling of the legs is common, and cardiac symptoms may also be present, being manifested by pain or oppression over the epigastrium with palpitation or irregularity of heart action.

The patient may remain in this condition for months or even years, with alternate improvement and exacerbation of symptoms. Such cases have been called *rudimentary or incomplete beriberi*, and such a history is frequently obtained from mothers whose infants have died of infantile beriberi. Usually the condition becomes progressively worse. The muscles become acutely tender to the touch, atrophy sets in, and as the wasting of the muscles continues the gait becomes altered and finally the patient is unable to walk at all. The legs are almost invariably affected first, but in many cases the muscles of the arms also become affected later and atrophy in the same manner. The muscles of the leg are affected before those of the thigh, and the muscles of the forearm before those of the arm. Finally, the patient becomes bed-ridden and quite helpless. Should there be no edema, the wasted form presents the picture of atrophic or dry beriberi.

In other cases, the muscular atrophy is much less marked, and is often masked entirely by the *extensive edema*. This edema is more intense and more frequent in the legs than in the arms, but such cases may develop marked general anasarca. Effusions of fluid into the pleura, pericardium and peritoneal cavity are common in this type which is generally called *wet beriberi*, and give rise to the usual symptoms and physical signs of fluid in these cavities. However, in most cases of this type, there is some degeneration of the nerves and the muscular atrophy resulting often proceeds to a considerable extent. Occasionally, for some unknown reason, possibly as the result of some change in the diet, one of these cases of wet beriberi begins to pass greatly increased quantities of urine, and in a few days the edema disappears, and the shrunken limbs and muscles stand revealed; the case has become converted into *dry beriberi*.

Both of these types of cases suffer from *cardiac symptoms* during the course of the disease. The patients complain of dyspnea, precordial pain and palpitation. The pain may be slight but is sometimes quite severe and may be the main reason for consulting the physician. These cardiac symptoms may be continuous, but are more often absent at times and occur in *paroxysms*, and such attacks occasionally increase in intensity until it is evident that the condition of the patient is serious. There is a horrible boring pain quite as severe as that experienced in angina pectoris, the patient gasps for breath, the face becomes cyanosed, the pulse becomes small and a venous pulse may appear in the neck. Often in the course of such an attack, the heart suddenly stops and the patient

is dead. Should he recover from this paroxysm, he may never have another acute cardiac seizure; but usually the dyspnea, pain and palpitation continue until sooner or later another paroxysm occurs and the patient dies. The mortality in beriberi is practically all caused by this sudden failure of the heart, and whenever beriberi is prevalent, there are numerous cases of sudden death among men who had not previously been supposed to suffer from the disease. Such sudden deaths have been common among native prisoners and native soldiers.

**SYMPTOMS PRODUCED BY DEGENERATION OF THE NERVOUS SYSTEM.**—These symptoms are mainly those of a peripheral neuritis, and may be classified as motor and sensory. The clinical picture depends upon which nerves are involved, but there is always a marked tendency toward involvement of the nerves of the extremities, particularly the legs.

*Motor Symptoms.*—These are caused by degeneration and weakness of the muscles supplied by the affected nerves. The extensors of the foot are usually first affected, followed by the muscles of the calf, the extensors and flexors of the leg. When the arms become involved, the muscles are affected in a similar order.

The muscles of the trunk are the last to become involved, while the muscles of the face seldom if ever suffer. As the muscles atrophy they become exceedingly tender to the touch, and their power to contract becomes progressively diminished so that great muscular weakness results. There may even be complete paralysis of certain muscles, but almost always the condition is one of weakness rather than paralysis. There may be contractions of the muscles or painful cramps.

*The Reflexes.*—The muscular reflexes are generally diminished or lost, though in early cases they may be slightly increased. The patellar reflex is the one that has been generally observed and it is normal or slightly increased in early cases, but in well-developed cases is practically always impaired and is frequently absent. The patellar reflex may be present in one leg and absent in the other.

*The Gait.*—This becomes changed as the muscles of the legs are involved, and is not characteristic, but depends upon which muscles are affected and the extent of the degeneration. Thus, in early cases, there may be toe drop with steppage gait; an ataxic gait and Romberg's sign are present in a considerable number of the cases. In more advanced cases, the patient merely shuffles about with the aid of a cane, and still later may become unable to walk at all. When the diet has been changed and convalescence has set in, the muscles become spastic and the gait then resembles that of spastic spinal paralysis. It is interesting to note that a similar spastic gait has been observed in fowls recovering from polyneuritis gallinarum as a result of treatment with extracts of rice polishings.

*Sensory Disturbances.*—The cutaneous changes consist of anesthetics with varying degrees of paresthesia, and the distribution of the anesthetic areas will depend upon the nerves involved. Anesthesia is common over the skin of the anterior surface of the leg. It may be complete, so that the prick of a pin is not felt at all, but more frequently it is partial

and the patient may report merely a touch instead of a sensation of pain. There is often also delayed sensation. Later in the disease, areas of anesthesia may appear upon the forearms, arms and trunk. Japanese authors describe an area of anesthesia about the mouth. Perception of heat, cold and pain are all diminished in the anesthetic areas. The paresthesias consist of sensations of pins and needles, numbness, formication and itching, and rarely these symptoms may be very troublesome.

**EDEMA AND SEROUS EFFUSIONS.**—The tendency to accumulation of fluid in the tissues is characteristic of the so-called wet cases of beriberi. The edema may be one of the first symptoms noted, or may be accompanied by various grades of polyneuritis. The edema usually appears first on the dorsum of the foot and progresses up the legs; less frequently it appears on the hands or face. It may remain localized or may extend to every part of the body. Associated with the edema are hydropericardium, hydrothorax and ascites. Hydropericardium is most frequent but may cause little trouble and is difficult to diagnose because of the hypertrophy of the heart, which is usually also present. Hydrothorax may be detected by the symptoms and physical signs of that condition. The amount of fluid may be considerable and cause much respiratory embarrassment. While there is generally an increased amount of peritoneal fluid in these cases, it is usually insufficient to cause pressure symptoms and is frequently overlooked during life. The fluid that accumulates in all these cavities is clear with a peculiar and characteristic yellow or greenish-yellow tint.

**THE CIRCULATORY SYMPTOMS.**—*The Heart.*—When the heart is affected, as it usually is, palpitation, epigastric pain and dyspnea are present in varying degrees. The apex beat is displaced downward and outward and percussion or fluoroscopic examination easily demonstrates that the heart is enlarged, usually to the right, and sometimes both right and left. Murmurs may be heard but they are not characteristic, are usually systolic, and are not due to valvular disease unless beriberi should be complicated by valvular disease of the heart. The second pulmonic sound is often accentuated and may be reduplicated. When the patient suffers an acute attack, the palpitation is accompanied by visible pulsation of the veins of the neck, he suffers a horrible pain about the heart and this is combined with a small, feeble, irregular pulse, low blood-pressure and cyanosis indicating the inability of the heart to move the circulation. The clinical picture combined with the pathological examination leads to the following conclusion: There is actual degeneration both of the pneumogastric nerves and of the myocardium resulting in weakness and derangement of the physiologic functions of the cardiac muscle. This is followed by compensatory hypertrophy, particularly on the right side. So long as compensation is thus secured all is well, but often the degenerated fibers fail and stretch, perhaps because of a sudden increase in the load on the right heart caused by some at present unknown pulmonary condition. The right ventricle dilates, followed by dilatation of the right auricle. If this dilatation is slow, it gives rise only to a moderate degree of palpitation,

pain and failure of the circulation; but when it occurs suddenly it causes the acute cardiac crises which so suddenly end in the death of the patient. This explanation of the mechanism suggests that venesection might give relief, and this has indeed been found to be the case. In the absence of cardiac symptoms, there is nothing characteristic in the pulse of the beriberic patient, except that it is apt to be small, easily compressible and irregular, as might be expected in a chronic myocarditis. It is to be hoped that the heart in beriberi may soon be studied by means of modern methods, including the electrocardiograph. At present such studies are lacking.

*The Blood.*—The blood has been much studied in this disease with the sole result that it has been determined that there are no characteristic morphological changes. There is apt to be a moderate anemia, but neither the red cells nor the hemoglobin are seriously reduced. The differential leukocyte count is either normal or shows a diminution in polymorphonuclear neutrophils and a corresponding increase in the lymphocytes, a condition found in many debilitated conditions. This finding confirms epidemiological and experimental investigations indicating that beriberi is not caused by an acute bacterial infection. Chemical changes in the blood have been insufficiently studied, but it has been shown that there is apparently a retention of urea as indicated by an increase in Ambard's coefficient.<sup>7</sup> This ranged from 0.06 to 0.08 in healthy cases, while in beriberi it varied from 0.07 to 1.36, and the two patients with the highest coefficient died. An increase in the non-proteid nitrogen of the blood has also been found.<sup>8</sup> These observations have not been confirmed, but they indicate that there is a disturbance of nitrogen metabolism. There is no important lesion in the kidneys to account for such changes, and the fact that the vitamin which prevents and cures this condition is a nitrogenous base, makes it seem probable that this vitamin is concerned in some way in nitrogen metabolism. Further studies on the nitrogen metabolism in beriberi are urgently needed.

**GASTRO-INTESTINAL DISTURBANCES.**—Gastro-intestinal disturbances are frequent. Vomiting is a constant and early symptom in the infantile cases, and occurs in the more serious cases in adults. Diarrhea and constipation both occur but constipation is more common and characteristic. It is probable that such disturbances are due to two factors: first, to the bulky carbohydrate diet usually consumed, and secondly, to the chronic passive congestion of the liver, stomach and small intestine following the damming back of the blood in the pulmonary circulation. Such congestion of the abdominal viscera is a common necropsy finding.

**URINARY FINDINGS.**—The quantity of urine is generally diminished, of low specific gravity, and the excretion of urea, uric acid and phosphoric acid is below normal. Albumin and casts may be found but are not constant and are probably dependent upon congestion of the kidneys as part of the general venous stasis of the abdominal viscera referred to above. There is no true nephritis and the edema is entirely inde-

pendent of kidney changes, being often found when the kidneys are apparently normal.

**APHONIA.**—In advanced cases both in adults and infants the voice is sometimes lost and the patient can only whisper. This is attributed to paralysis of the muscles of the larynx as a result of degeneration of the pneumogastric nerves.

**Differential Diagnosis.**—Beriberi must be distinguished from the other forms of peripheral neuritis caused by the various intoxications such as alcohol, arsenic, and lead. This can usually be done by the history and the absence of edema in cases of toxic polyneuritis. The history of a deficient diet can be elicited in beriberi if the investigator is thoroughly familiar with the articles of diet that are deficient in antineuritic vitamin. Heart disease and nephritis must also be excluded. In cardiac disease there are often valvular lesions. Simple myocarditis is more difficult to differentiate, but in beriberi the degeneration is associated with hypertrophy, and in ordinary cardiac lesions the symptoms of peripheral neuritis will be absent. In nephritis albumin and casts are found in the urine with regularity, and blood-pressure is generally increased, while in beriberi it is normal or decreased; and again the symptoms of peripheral neuritis do not occur in nephritis. The combination of peripheral neuritis with edema and hypertrophy and degeneration of the myocardium forms such a characteristic group of symptoms that the diagnosis is really easy in the majority of cases if the existence of beriberi is once suspected; but in countries where beriberi rarely occurs, such cases have often gone undiagnosed for months. On the other hand, in the early days in the Philippines, certain cases of alcoholic neuritis in soldiers were erroneously diagnosed as beriberi.

When beriberi has once appeared among a group of men on a similar diet such as the inmates of a prison or a group of soldiers or laborers, if all the members of the organization are carefully examined it will be found that many of them suffer from some weakness of the legs, anesthesia over the tibiæ, or a loss of patellar reflexes. It is among such cases of rudimentary or latent beriberi, who go about their duties and have been supposed to be normal, that sudden unexpected deaths from cardiac failure occur. Therefore, when beriberi has occurred, the responsible medical officer should test all members of the organization. A large number of men may be examined rapidly by applying several simple tests:

(1) Squeeze the muscles of the calf to detect muscular hyperesthesia. Healthy muscles will stand a good deal of pressure without causing any pain.

(2) Test the anterior surface of the leg with a pin for anesthesia. Men who are developing beriberi can often be prodded until the blood runs without feeling pain.

(3) Test the patellar reflex. Any modification is suspicious.

(4) Perform the squatting test. The patient squats upon his heels in the oriental manner. In the beriberic this may cause pain, and he may be unable to rise except by using the hands to pull the body up.



**Complications.**—In uncomplicated cases there is no fever. The frequency with which fever does occur is an indication of the frequency of intercurrent infections to which such patients are especially susceptible. Bronchopneumonia is frequent and often found at necropsy. Malaria and intestinal infections also occur. The close association of beriberi and scurvy in so-called ship beriberi has been referred to in the article on scurvy.

**Pathology.**—The entire nervous system is profoundly altered. Degeneration both of the sheath and the axis cylinder of the peripheral nerves may be demonstrated by appropriate staining methods. Similar changes have been found in the pneumogastric nerve and the fibers of the sympathetic system. Sections through the spinal cord show a diffuse degeneration of the fibers of all the tracts. The cells of the anterior horn show changes consisting usually of chromatolysis. The tigroid substance which usually appears throughout the cell as a skein or network of material stainable by Nissl or Giemsa stains, disappears or remains only as a little granular material grouped at one end of the cell, while the remainder of the cell is clear and unstained. Evidences of nuclear degeneration are also found in more advanced cases. Similar degenerative changes have also been found in the cells of the sympathetic ganglia. Funk<sup>9</sup> has found marked chemical alteration in the brains of fowls suffering from polyneuritis gallinarum, and Lhermitte<sup>10</sup> has found marked lesions in the cells of the brain, with progressive disintegration associated with proliferation of the neuroglia. It should, therefore, be evident that although the symptoms are chiefly those of a peripheral neuritis, the condition is not a simple polyneuritis but a degeneration of the entire nervous system. There are, however, no mental symptoms and the mind remains clear.

Corresponding changes are found in the muscular system. In the gross the muscles are wasted, and the primary change found microscopically is a diffuse parenchymatous degeneration combined at times with fatty and hyaline degeneration.

The heart is practically always hypertrophied, and this may be combined with dilatation. This change is most marked in the right side of the heart though the left side may be similarly affected. The myocardium shows fragmentation of the muscle fibers with hyaline and fatty degeneration. The bundle of His has been shown to be implicated in certain cases, and degeneration of the intramural nerves has been reported. From these findings the cardiac symptoms are explainable.

Varying degrees of pulmonary edema are found. In the wet cases some of this may exist during life, but for the most part it is an agonal change due to the failure of the heart. Subpleural ecchymoses are frequent. Some bronchopneumonia may be found though this is due to complications rather than beriberi.

Chronic passive congestion of the abdominal viscera is a usual finding. There may be a typical nutmeg liver. The mucosa of the stomach and duodenum is congested and ecchymoses into the mucosa in these localities are frequent. It was this congested duodenum that led Hamilton Wright

to explain beriberi as an infectious duodenitis. The kidneys are also often greatly congested.

Combined with these findings are anasarca, hydropericardium, hydrothorax, and ascites in a varying proportion of cases depending upon the predominance of the "wet" type of the disease. Hydropericardium may be found in 75 per cent. of the cases, anasarca and increased peritoneal fluid in 50 per cent. In one set of necropsies, hydrops of all the serous cavities occurred in 20 per cent. of the cases. The fluid found is yellowish or greenish yellow, clear, and may be in considerable amount.

**Treatment.**—PROPHYLAXIS.—Beriberi chiefly occurs among the native races of tropical or sub-tropical countries where it is caused by the too exclusive use of highly milled or decorticated rice. To a lesser extent, it occurs in institutions or among troops whose ration is deficient for various reasons.

Beriberi may be prevented among such native races either by the substitution of an undermilled rice for the decorticated rice previously used, or by the addition of other beriberi preventing articles, such as peas, beans or barley, to the ration. Both of these methods have proved successful among troops or in institutions under governmental control. Both are difficult to enforce in the civil native population.

When an undermilled rice is introduced for the prevention of beriberi, each lot purchased must be examined to be sure that sufficient of the external layers of the grain remain. This may be accomplished by inspection after staining, or by a chemical examination. If rice is stained with Gram's iodine solution, the starch turns black on contact with the iodine. A decorticated rice from which the external layers have been removed and only the starch remains, becomes entirely black; an undermilled rice may show some black spots, but the greater part of each grain will remain unstained and will be yellowish-white or red according to the color of the external layers of the grain which protect the starch from the action of the iodine. With a little experience, a beriberi preventing rice can easily be selected by this method.

The greater part of the phosphorus of the grain is present in the external layers, and is removed in the polish in the production of decorticated rice. The amount of phosphorus pentoxid remaining in the rice has therefore been used as an indicator to show how completely the external layers have been removed. It has been found that any rice that contains at least 0.4 per cent. of phosphorus pentoxid, contains sufficient of the external layers to prevent beriberi.

With regard to the addition of other foods to a ration consisting of beriberi producing rice, it should be noticed that the Japanese prevented beriberi by mixing ten ounces of barley with 20 ounces of rice. Four ounces of peas or beans daily has also been found to protect men whose diet otherwise consisted practically exclusively of beriberi producing rice. The difficulty with these measures is that among a large group of men there will always be found a few who will refuse to eat the articles provided to prevent beriberi. Moreover, peas and beans become very tiresome when used continuously. With the addition of a

reasonable amount of eggs, meat or milk, the amount of peas or beans that must be consumed can be considerably reduced. From much practical experience and experimental evidence it may be concluded that beriberi may be completely eradicated from any institution or body of men by the observance of the following precautions:

(1) If rice is the staple it should be undermilled. Similarly when bread is the main staple it should be made from whole wheat flour or whole cornmeal.

(2) Beans, peas or similar legumes should be served once a week.

(3) Barley should be used in soups.

(4) Fresh meat should be served once daily if possible. Certainly twice weekly.

(5) The too exclusive use of canned foods must be avoided.

Native races not under government control must be led by education to make similar changes in or additions to their diet. The sale of undermilled rice, in place of the highly milled or decorticated rice which produces beriberi, should be encouraged by the government. It has been suggested that this may be done by placing a tax on the decorticated rice which should be sufficient to make its cost prohibitive for the native poor, who would then be compelled to purchase the undermilled rice which would be cheaper and which would protect them from beriberi.

**MEDICINAL TREATMENT.**—The treatment of beriberi is unsatisfactory. As the condition is due solely to a dietary deficiency, there are no drugs that afford any specific benefit; but some are useful in the relief of certain symptoms. To overcome constipation, a frequent symptom, the **saline cathartics** are probably superior, particularly in cases of wet beriberi where they may encourage the abstraction of water from the tissues. Pain may be relieved by the use of **bromids and anodynes.** **Strychnin** appears to have some value as a **general tonic**, and is widely used. While not curative it has been found to prolong the life of experimental animals.

As death is generally due to cardiac failure, the heart condition should receive careful consideration. If there is any evidence of cardiac symptoms or circulatory embarrassment, such patients should be kept in bed and **digitalis** given in full doses. If cardiac failure appears imminent, **venesection** is indicated. The abstraction of blood relieves the overdistention of the dilated and laboring heart and may enable it to tide over the critical moment. The beneficial results of venesection in this condition have been affirmed by many authorities.

**DIETETIC TREATMENT.**—The real treatment of beriberi is dietetic. All adult cases should be given a full and varied diet having especial care to include a number of articles known to be rich in antineuritic vitamin, and to exclude deficient articles. Thus decorticated rice should be prohibited, though in deference to the tastes and habits of native patients a limited amount of undermilled rice may be permitted. Meat, eggs and milk should be used freely, and beans, peas and barley should be used to as great an extent as possible. Canned foods should be rigidly excluded, and meats and vegetables should not be cooked to excess; meats should be served rare.

Either yeast or rice polish may be given. These substances are rich in antineuritic vitamin, but are unpleasant to take and disturb some stomachs. To avoid this, an extract of rice polishings may be used to good effect. This may be made by extracting the polishings with three to six times their bulk of alcohol (90 per cent.) evaporating off the alcohol in the cold by the use of an electric fan, discarding the fat which separates out when the alcohol is evaporated, and redissolving the syrupy residue in a small amount of water. This extract has been found to possess great curative powers in cases of infantile beriberi, and the Philippine legislature has for several years made an appropriation to provide for the preparation of this extract and its distribution to cases of infantile beriberi among the poor. Such an extract is of considerable value in the treatment of many adult cases. An adult should receive the extract from about a kilogram of polishings daily, and infants a similar amount in proportion to their body weight. When properly prepared, the extract is non-toxic, is pleasant to take, and does not derange the stomach. It should be tested on animals before using on patients, for if improperly prepared it may be poisonous.

**Prognosis.**—If the deficient diet be maintained, the mortality in outbreaks of beriberi may be very high. Thus in some outbreaks mortalities of from 50 to 75 per cent. have been reported. This is exceptional, and the average mortality of the cases of beriberi in the community as a whole will probably be about five per cent. In hospitals where only serious cases are admitted, it may reach 20 per cent.

From this it will be seen that recovery in any given case is by no means certain, and a guarded prognosis should be given in any serious case. However, if a proper diet be furnished, and especially if the extract of rice polishings be used, the mortality should be small, and all but those cases in a critical condition when admitted to the hospital should be saved.

Unfortunately, so far as adults are concerned, recovery is apt to be slow, and is often a matter of weeks and sometimes months. The damage that has been done to the nervous system cannot be repaired at once even though a diet rich in vitamins be given. Nor does this afford any evidence that the disease is not caused by dietary deficiency. The deterioration of the nervous system is gradual, and has proceeded for months before clinical symptoms appeared. The return to normal is likewise a slow process. The tendency for the development of a spastic gait during recovery was mentioned before. It frequently makes walking exceedingly difficult and to some extent masks the progress that the patient is making.

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## CHAPTER XII

### PELLAGRA

By JOSEPH GOLDBERGER, M.D.

Synonyms, p. 205—Etiology, p. 205—Infectious versus dietary origin, p. 206—Predisposing causes, p. 210—Symptomatology, p. 212—Clinical history, p. 212—Mode of onset, p. 212—Course, p. 213—Individual symptoms during course of the disease, p. 214—Pseudo-pellagra, 223—Diagnosis, p. 223—Complications, p. 225—Sequelæ, p. 225—Association with other diseases, p. 225—Clinical types, p. 226—Treatment, p. 226—Preventive, p. 226—Curative, p. 227—Local, p. 228—Climatology, p. 228—Medicinal, p. 229—Prognosis, p. 230—Pathology, p. 231—History, p. 231—Distribution, p. 233—Bibliography, p. 233.

**Synonyms.**—The name "pellagra" is in current use in the medical literature of practically all countries. One finds in addition, particularly in the older literature, many other names for the most part popular local designations, among which may be cited the following:

(Egypt) Qusshuf; (France) Brûlure, Dartre maligne, Maladie de la teste, Mal de St. Amans; (Italy) Mal del sole, Mal del padrone, Malla-tia della miseria, Salso, Scorbuto alpino; (Spain) Mal de la rosa, Mal del higado, Flema salada; (Roumania) Buba trinjilor, Rana trinjilor, Boala seracilor (Disease of the poor).

**Etiology.**—An enormous amount of effort has been directed to the elucidation of the cause. Many suggestions have been made and theories advanced; only the most important can be considered.

Among the earliest suggestions was the rather vague and indefinite one that pellagra was due to bad food. This was followed by the theory, advanced by Marzari (1810), that corn (*Zea mays*), by reason of its supposed poverty in protein, was the cause of the disease. This view was further elaborated by Lussana and Frua (1856), who regarded pellagra as due to an "insufficient neuromuscular repair resulting from a deficiency of protein in maize" (Roussel), but was discredited by the demonstration that corn compares favorably with other cereals in protein content and other nutrients.

The inadequacy of Marzari's (the original zeistic) theory led to the elaboration of the toxicochemical or spoiled corn theory with which the name of Lombroso is principally associated. According to this, pellagra is an intoxication due to the ingestion of poisonous substances developed in maize as the result of the action of microorganisms in themselves harmless to man. Up to within a few years this theory was well-nigh universally accepted and was made the basis for the prophylactic measures adopted by the Italian and the Austrian Governments.

The various theories based on corn as the essential determining factor are untenable in view of the occurrence of cases in which corn formed no part of the diet. The alleged reduction of pellagra in Italy following the inauguration of measures based on the spoiled maize theory, probably the weightiest evidence adduced in its support, may be interpreted, however, as due to the operation of other coincidental factors, chiefly of an economic character; in any event, it can be interpreted at most as indicating that corn (sound or spoiled) may be a factor, though not necessarily an essential one, in the production of the disease.

In 1905, Sambon suggested and, later (1910), elaborated the theory that pellagra is an insect-borne parasitic disease the transmitting agent of which is some species of *Simulium* or buffalo gnat. The occurrence of the disease in localities from which the *Simulium* is absent and the complete exemption of employees (officers, nurses and attendants) at institutions in which it has long been endemic render this and other similar theories untenable.

The failure of previous theories and the analogy to beriberi led Funk (1912) to advance the theory that pellagra is due to a deficiency in the diet of a substance belonging to a class named by him "vitamin." According to this author, this deficiency is most commonly brought about by the consumption of corn in the milling of which the vitamin-bearing portion of the kernel has been removed, but he points out that the deficiency may be brought about in other ways. He recommends potatoes, meat and fruit as vitamin-rich foods for the control of the disease. While much may be said in favor of this attractive theory, it still lacks demonstrative proof.

In 1913, Alessandrini and Scala advanced the theory that pellagra is an intoxication with colloidal silica contained in drinking water which has been in contact with a clay soil. They stated that in Italy the disease is sharply restricted to localities where such water is used. The peculiarities of distribution of the disease as observed in the United States afford no support to this interesting theory. In fact, the rather sharp limitation of the disease to certain sections of populations having a common water supply would seem to be fatal to the theory.

INFECTIOUS VERSUS DIETARY ORIGIN.—Following the recognition of the widespread prevalence of the disease in the United States, a conviction of the inadequacy of the older etiological theories rapidly developed. This led to a reëxamination of the whole question with the development of two opposing views of the nature of the disease, namely, (a) that the disease is an infection in which diet plays a more or less important but not an essential rôle, and (b) that the disease is essentially of dietary origin, a faulty diet being the primary factor in its causation.

(a) The reasons that suggest themselves or have been advanced by American students for regarding pellagra as an *infectious disease* may briefly be summarized as follows:

(1) The seemingly abrupt appearance of the disease in the United States, its apparently rapid extension and progressive increase and, in

the main, its rather sharp limitation to the southern, warmer part of the country;

(2) The marked seasonal character of the disease;

(3) Its markedly higher incidence in women than in men;

(4) Its association with unsanitary conditions (Thompson-McFadden Commission);

(5) Evidence of close association with a preëxisting case in a high percentage of cases (Thompson-McFadden Commission; Jobling and Petersen);

(6) Evidence that the disease may be controlled by improved sanitary conditions (Thompson-McFadden Commission);

(7) Its occurrence in the well-to-do, in those with a liberal diet available, and in well-nourished individuals.

(b) The principal reasons for considering pellagra as primarily of dietary origin have been summarized by Goldberger and Wheeler as follows:

“(1) In institutions for the treatment of pellagra (‘pellagrosario’ or hospital), employees (nurses and attendants) in constant contact with the disease practically never contract it while so employed.

“(2) It has been found that employees (nurses, attendants, etc.) resident in institutions in which pellagra is and has for long periods been endemic (occasionally also epidemic) and many of them also in frequent or constant contact with cases of the disease, practically never contract it while so employed. This exemption has been found associated with a decided difference in diet and in no other significant respect.

“(3) Active cases of pellagra respond promptly and strikingly to an appropriate diet. Exceptions are relatively rare and no more than might be expected when the experience in beriberi and scurvy is kept in mind. The natural tendency to recovery from the attack without change of environment and without therapeutic interference is associated with a significant seasonal change in diet.

“(4) Pellagra may be prevented completely by a suitable diet without intervention of any other known factor, hygienic or sanitary. There is no sound evidence that the disease is controllable in any other way.

“(5) Attempts to transmit the disease to the human subject by inoculations of blood and of nasopharyngeal secretions, and by feeding with dermal scales, urine and feces from cases of pellagra in various stages and of varying degrees of severity, were without result. The report by Harris of a successful inoculation of a monkey with a filtrate from pellagrous lesions remains unconfirmed, although extensive attempts have been made, notably by Lavinder and Francis and by Harris himself.

“(6) Chittenden and Underhill have by feeding succeeded in producing pellagra-like symptoms in dogs.”

In addition, Goldberger and Wheeler carried out a successful feeding experiment on convicts in Mississippi. The diet was derived from wheat



flour, maize meal, grits and starch, rice, Irish and sweet potatoes, some green vegetables, pork fat, sugar and syrup. At the end of five and a half to six months at least six of the eleven convicts developed convincing evidence of pellagra, while of a large number of controls none showed any indications of the disease.

In estimating the weight and significance to be attached to the available evidence relating to the nature of the disease account should be taken of the following considerations:

Of the reasons advanced above in favor of infection, 1 and 2 are equally consistent with a dietary view of its origin. The literature of scurvy and of beriberi affords numerous striking analogies to every point raised. It may also be stated that there are good reasons for believing that, as the result of the operation of changing industrial and economic conditions in the South during the past twenty-five or thirty years, the diet of an increasing number of people of that section of the country has been unfavorably influenced, the unfavorable influences being particularly accentuated since 1907 (Sydenstricker).

The markedly higher incidence of the disease in adult women is not readily accounted for from either point of view. The suggestion that women are less resistant than men is consistent with both. In the eventual explanation of the interesting phenomenon under consideration, from the point of view of diet, account will have to be taken of the possibility (*a*) that the adult female (a menstruating and child-bearing animal) may have some physiological requirements that are different either in degree or in kind from those of the male; (*b*) that the period of development of the disease may be somewhat longer in the male than in the female, so that the progress of the disease to full development in the former is more often blocked by changes in diet incidental to the changing seasons; (*c*) that, as the result of the interplay of social factors in an environment of poverty, there may develop a disposition to maintain the diet of the wage-earner (and child) at the expense of the housewife or mother; (*d*) that the diet of women is more likely to be affected by individual eccentricities resulting from various psychic factors to which women generally, and the housewife more particularly, are more sensitive than men.

As a disease of poverty it may naturally be expected to be associated with unsanitary conditions; there is no good evidence that this association is other than accidental.

The evidence of close association with a previous case has all been collected in endemic areas of high prevalence and as there is good reason to believe that this may be purely fortuitous, and as there is no sound evidence to the contrary, this argument for infection is without any real weight.

The only available direct evidence that the disease may be controlled by improved sanitary conditions is based on the result of one experiment carried out by the Thompson-McFadden Commission. Pellagra is reported by this Commission to have disappeared from a cotton-mill village of South Carolina following the installation of a water-carriage

sewerage system. This, however, has been shown by Goldberger and Wheeler (1920) to have been an error, so that there really exists no sound evidence that the prevalence of the disease can be controlled by improving sanitary conditions.

Its occurrence in the well-to-do and in such as seem to have a good diet available has been interpreted repeatedly as indicating that the disease may occur in one subsisting on a good diet, the fact being overlooked that having a good diet available and consuming it are not necessarily synonymous. Precisely the same argument may be found repeatedly advanced in the literature of scurvy and of beriberi against diet and in favor of infection in these diseases. The difficulty of determining in a particular instance as to whether a diet is adequate or not is so very great (1) by reason of the practical impossibility of obtaining accurate detailed information as to the actual composition of the diet consumed, (2) by reason of the meagerness of our fundamental knowledge of foods and diets, and (3) by reason of the well-known certain occurrence of borderland cases, that general statements of the occurrence of cases in individuals with a good diet available can have little or no evidential value. In reality, in a high proportion of such cases very suggestive or clear indications of the consumption of a restricted diet may be secured.

The occurrence of the disease in individuals to all outward appearances well nourished would seem to be inconsistent with a dietary origin of the disease. This seeming difficulty sinks into insignificance when it is recalled that scurvy and beriberi may occur in apparently well-nourished individuals.

Goldberger, Wheeler and Sydenstricker have studied the diets of non-pellagrous and of pellagrous households, and report their results in part as follows:

"(1) The pellagrous households had a more restricted supply of the foods of the 'animal protein' group (lean meat, milk including butter, cheese and eggs).

"(2) Increasing supplies of milk or of fresh meat were found associated, one independently of the other, with a decreasing pellagra incidence.

"(3) The fuel supply of the diet would seem in itself not to be an essential factor in relation to the incidence of the disease.

"(4) A deficiency in total protein would seem not to be an essential factor in relation to the incidence of the disease.

"(5) The protein mixture (amino-acid supply) in the diets of the non-pellagrous households is more likely to be physiologically adequate than that in the diets of the pellagrous groups.

"(6) The supply of carbohydrate was, if anything, somewhat smaller in the diets of the pellagrous than in those of the non-pellagrous households, so that the production of pellagra would seem not to be dependent on the excessive consumption of this nutrient.

"(7) The diets of the pellagrous households have a smaller average.

supply of the recognized vitamins than do those of the non-pellagrous, the disparity in the supply being particularly marked with respect to the 'fat-soluble A' factor.

"(8) The mineral makeup of the diets of the non-pellagrous households will tend to be superior to, or at least is less likely to be deficient either as a whole or in any of its elements than that of the pellagrous households.

"(9) The indications afforded by this study suggest that the pellagra-producing dietary fault is the result of some one or of a combination or combinations of two or more of the following factors:

"A physiologically defective protein (amino-acid) supply.

"A defective or inadequate mineral supply.

"Deficiency in an as yet unknown dietary essential (vitamin?)."

McCollum's analyses, by the biological method in rats, of diets regarded as pellagra-producing have led him to much the same interpretations, except that he does not believe that a specific vitamin is concerned, his studies having led him to the conclusion that but two vitamins are necessary in mammalian nutrition. The more recent conclusive demonstration of a third, an antiscorbutic, factor would seem to weaken somewhat his contention against the possibility of a specific vitamin playing an essential rôle in this disease.

In *summary*, it may be stated, on the one hand, that there exists no unequivocal evidence in support of the conception of an essential infective factor in the causation of the disease; while, on the other hand, the controlling influence of diet in the causation and in the prevention of the disease has been conclusively demonstrated; the exact dietary factor or factors constituting the specific pellagra-producing fault is undetermined, but is to be sought in some one or some combination or combinations of the following: (a) a physiologically defective protein (amino-acid) supply, (b) a defective or inadequate mineral supply, and (c) a deficiency in an as yet unknown dietary essential (vitamin?).

PREDISPOSING CAUSES.—The disease occurs not only sporadically but also epidemically and endemically under widely contrasting conditions of climate, soil, altitude and source and character of water supply. Each of these factors has at one time or another been considered as of primary importance in relation to the etiology of the disease. That the relation is accidental and at most of secondary importance is evidenced by the fact that the disease is or has been highly prevalent under such diverse conditions as those represented by northern Italy, South-Tyrol, Transylvania, Bukovina, Rumania and Bessarabia on the one hand, and Lower Egypt, West Indies and Yucatan on the other. The much higher incidence of the disease in the southern than in the northern and western parts of the United States must, therefore, be related primarily to some factor or factors other than climate. It may here be noted that a difference in diet, that of a lower consumption of the animal foods in our Southern States, has long been recognized.

Both sexes are attacked, but in the United States the incidence is very

much higher in the female than in the male. A higher incidence for males than for females has been reported for some other countries (Scheiber). The disease has been observed in individuals at all periods from infancy to old age. Cases in children under two years, however, are relatively rare, and in infants less than one year old, very rare indeed. It has been observed in nursing infants whose mothers were apparently free of the disease, but much more commonly the nursing child shows no recognizable manifestations though the mother may present well-marked evidence of the disease. In the United States the incidence in *adult females* is several times as high as it is in adult males but both under 20 and over 45 years the incidence in the two sexes is about equal.

The disease is highly prevalent in the United States in both the white and the negro *races*; in some localities the former, in others the latter, is preponderatingly affected. Jews are stated to be less frequently affected than others in Rumania and this has also been claimed for the United States.

*Heredity* was long regarded as playing an important rôle. Elizabeth Muncey, in an investigation of the question, failed to find evidence of direct heredity. The seeming tendency of the disease to occur in successive generations and in certain families may be regarded as largely the expression of the fact that the disease is closely bound up with poverty. Heredity has been invoked to explain the origin of certain cases without maize that could not be disposed of by the easy method of calling them "pseudo-pellagra."

From the earliest history of the disease it has been observed that its incidence is closely bound up with the *condition of poverty*, and that its prevalence is notably influenced by fluctuations in economic conditions. In Mississippi approximately 11,000 cases were reported for 1914, but in 1915, following the great depression in the price of cotton, the staple crop in that State, brought about by the outbreak of the World War, the number of cases jumped to approximately 16,000. The rise of the price of cotton in 1915 and the consequent improvement in economic conditions were followed by a drop in reported cases to somewhat under 8,000 for 1916. Similarly, in the United States registration area for deaths the rate of 2.3 per 100,000 for 1914 jumped to 4.2 for 1915, and receded to 3.3 for 1916.

In Europe and in Egypt this disease has been reported as being confined almost exclusively to the *rural population*. In the United States the disease is not so sharply restricted to the country as would seem to be the case abroad. In this country the disease seems particularly prevalent in certain rural areas and in the small, more or less isolated, *mining and saw-mill camps and cotton-mill villages of the South*. It is of frequent occurrence in insane asylums, orphanages and prison camps, but in these the disease is almost absolutely confined to the inmates, officials and employees almost never being affected. Unlike scurvy and beriberi pellagra was not known before the World War as a disease of navies or armies even of countries in which it was highly endemic, as in Italy and Egypt.

As might be expected from a disease of poverty and from the fact of its occurrence in small communities such as saw-mill and mining camps and cotton-mill villages, in most of which sanitary conditions are of the crudest character, the disease is frequently associated with *bad hygienic and sanitary conditions*.

*Pregnancy and lactation* have repeatedly been stated to favor the development of an attack, but, while this may indeed be the case, the facts on which this is based hardly warrant this interpretation without considerable reserve, inasmuch as it is not clear that the association may not be a chance one, resulting from the high incidence of the disease in women at an age period when pregnancy and lactation are also of frequent occurrence.

It has been observed that *surgical operation* has in some instances been followed within two or three days by the development of well-marked evidence of pellagra in individuals previously apparently free of the disease. Whether such cases are simply instances of a chance coincidence or whether the shock or strain of the operation in some way hastened the development of a larval into a frank attack cannot be stated.

*Alcoholism* has at times been regarded as an important predisposing factor, and on the other hand many observers, including Roussel, regarded a shortage of wine in the diet as an important factor in the production of the disease. The association of alcohol with the disease can, in general, hardly be regarded as other than a chance one. In individual instances, by interfering with appetite and proper food intake, chronic alcoholism or the chronic gastritis caused by it may favor the production of the disease.

In asylums for the insane the disease occurs most commonly in the demented and the deteriorated.

Various factors by unfavorably influencing the diet of the individual may operate as indirect or predisposing causes, among which may be mentioned disagreeable visual (psychic) impressions, such as seeing a beef slaughtered or a fowl decapitated, which may make such food highly distasteful, and conditions of the mouth, such as loss of teeth or pyorrhea, making chewing difficult or painful, thus leading to the eating of soft mushy mixtures and the avoidance of those, such as meat, requiring mastication.

**Symptomatology.**—It is customary for systematic writers to describe the disease as passing through successive stages, such as first, second, third and fourth or præruptive, eruptive, cachectic, etc. Such divisions are highly artificial and the advantage of convenience which they afford is offset by the misleading impression that is conveyed. The following description of the clinical course is based principally on the writer's own observations in the field, at the U. S. Pellagra Hospital, Spartanburg, S. C., at asylums, orphanages and on the cases experimentally produced by the writer in association with Wheeler.

**CLINICAL HISTORY.**—*Mode of Onset.*—The disease begins in almost all instances with some diminution of strength; this, however, may be

so slight or the decline be so gradual and extend over so long a period that the patient himself may not fully appreciate the fact. With the decrease in strength there is almost always some loss of weight.

With the growing weakness there frequently appear various nervous manifestations, such as headache, disturbed sleep or insomnia, "nervousness" and dizziness.

Symptoms of indigestion, such as gaseous or acid eructations, discomfort after eating, epigastric or precordial pains, are frequent and early in adults, but apparently rare in children. The appetite may become dulled or capricious, but frequently appears unchanged and in rare instances may appear much increased. At first the bowels tend to be constipated or to act with normal frequency; in a small proportion of cases, a tendency to irregularity with occasional looseness of the bowels develops.

After a variable time a sensation of burning in the mouth, with or without some redness, may appear. The redness at first most commonly affects the tip, or the tip and margins of the tongue; less frequently the buccal mucosa becomes more or less evenly reddened.

In a very large proportion of all cases, after an irregular period during which some or all of the foregoing symptoms have developed in some degree, an eruption characteristic of the disease makes its appearance.

*Course.*—The further course of the attack varies. In the vast majority of cases seen in endemic areas, the symptoms, having begun in the late winter or early spring, attain at most a moderate degree of severity in the course of the succeeding two or three months. After continuing without much change for a few weeks, they begin to subside, the eruption as a rule being the first to disappear. Thus the eruption most frequently makes its appearance in May, June or July, but is gone by August or September. When untreated, or improperly treated, a return to the standard of health *normal to the individual* may not take place for several months, that is, not until late in the fall or early winter.

In a small proportion of cases, the severity of the attack becomes progressively more marked, especially as relates to the gastro-intestinal tract or nervous system or both, and, after a variable time, may reach a fatal termination, or, after remaining in a serious or critical condition for a shorter or longer period, the patient improves and gradually regains his customary health.

After this the individual may (1) continue through life in good health, (a) without any indications of having passed through a possibly serious illness, or (b) with only dermal residuals as evidence of a previous attack; (2) may continue to complain for long periods, possibly through the rest of his life, of more or less vague nervous manifestations, sequelæ of the attack; or (3) the cycle is repeated, a more or less fully developed attack recurring in the spring of the next succeeding or some subsequent year. If not interfered with a recurrence in the immediately succeeding year may be expected in roughly fifty per cent. of cases. This rate as well as that for new cases is markedly influenced

by economic conditions; good times being followed by a reduction; hard times, by an increase.

*Individual Symptoms during Course of Disease.*—(a) *Strength.*—The most nearly constant and perhaps earliest subjective manifestation of the disease is some degree of diminution in strength, a sense of weakness which is frequently referred to the legs. In many instances this is very slight or not definitely appreciated by the patient himself. On the other hand, it may be the sole complaint of the patient for long periods. Clinically such patients complain that they find it an increasingly great effort to attend to their usual duties. At first the sense of weakness may be accompanied only by mild nervous manifestations; later it may also be accompanied and be accentuated by diarrhea.

(b) *Weight.*—Some loss of weight is almost as frequent a manifestation as is a diminution in strength. It does not always occur or it may be very slight and clinically not always recognizable unless the patient has been in the habit of regularly weighing himself or for some reason has been weighed. Some patients may appear to be well-nourished and perhaps quite obese, but many, if not quite all of these, have probably lost some weight. The loss of weight may be very marked from the outset and may become extreme in advanced so-called cachectic cases.

(c) *Gastro-intestinal.*—A burning sensation in the mouth is a not infrequent and sometimes a fairly early complaint. Less often the burning also involves the pharynx and occasionally extends along the esophagus. More rarely the patient may complain of a sensation of burning from mouth to anus as if the entire tract were “raw.”

The burning in the mouth is frequently accompanied by a redness of the tongue or mouth. The redness, when it occurs, ordinarily appears first at the tip or tip and margins and usually is slight, sometimes very slight. Less frequently it involves the entire dorsum of the tongue and more rarely the entire buccal mucosa. In the slighter grades of involvement the tongue is clean and unusually red. In more marked cases the epithelial surface may be denuded and the tongue appear flaming red, at times like raw beef—the beefy tongue. The buccal mucosa may be similarly affected and may appear diffusely red or present flaming red patches over which the epithelial layer may appear as a gray somewhat slimy, fairly easily detached pseudo-membrane. The reddening of the mouth may extend to the cutaneous border of the lips, the purplish red inflamed appearance of which may in the insane be the first thing to arrest the attention of the observer.

With or without the inflamed condition of the mouth an increase in the salivary flow may at times be observed; in relatively very rare instances this increase may be so great that there is a constant drooling of saliva. Sullivan and Jones have found the sulphocyanate content of the saliva in this disease much less marked than in normal people. The sense of taste is in some of the more marked cases altered so that everything seems to be abnormally salty. In the severer cases one

asionally meets with fissuring at the oral commissures with or without some erosion of the skin.

(d) *Appetite*.—The appetite in a very large proportion of all cases is not notably affected. It may, however, be diminished to a varying degree, or, in rare instances, may be considerably increased, the patient complaining of always being hungry. A tendency to nausea may appear early and may be accompanied by vomiting; as a rule, however, nausea is a notable symptom only in some advanced cases when it may be accompanied by severe or intractable vomiting. Symptoms of indigestion such as gaseous or acid eructations and gastric or abdominal discomfort after eating are frequently met with as early symptoms in adults. The secretion of hydrochloric acid is suppressed in many cases.

Contrary to common impression, the bowels, as a rule, act normally or tend to be constipated. Less frequently there is a tendency to some looseness of the bowels; this appears mainly in advanced though not necessarily long-standing cases, but may be an early symptom. The looseness may be irregular and variable in degree, the stools becoming either soft or mushy, or watery in serious cases. The diarrhea, in some cases distinctly nocturnal, may be so severe as to lead to death through exhaustion.

(e) *Nervous System*.—Vague, ill-defined nervous symptoms are of common occurrence and may be among the very early manifestations of the disease. The complaint of "nervousness" is probably the most frequent and among the earliest, if not the earliest. Dizziness, frequently described by the patient as a "swimming in the head," or, by reason of the unsteadiness in gait which it may cause, as "blind staggers," is a fairly frequent complaint. Headaches, diffuse or variously localized, are quite common; some degree of insomnia is of almost as frequent occurrence. Various pains, of a somewhat neuralgic character, are not uncommonly encountered. Of these, a pain in the left side of the chest is perhaps the most common and most characteristic. Pains in the feet or feet and legs, at times very severe, may be met with. Epigastric or abdominal pains, cramp-like or sharp, may occur and be so severe and in some cases appear so localized as to give rise to suspicions of abdominal disease. These may at times lead the unwary to the performance of exploratory operations.

Paresthesias are fairly frequent and at times appear quite early. Of these, burning of the hands or of the feet is fairly characteristic and may be very annoying and persistent. The knee reflex is in most instances unchanged; frequently, however, it is increased, less often diminished.

Irritability or dullness and apathy may be met with. Milder degrees of these are not easy to determine and may not be appreciated until after a course of treatment, when the change may be very striking.

The mental faculties may be affected, but fortunately this happens much less frequently than is ordinarily believed. Disturbances of a degree calling for institutional care probably do not occur in over two or three per cent. of cases. The mental manifestations associated with



pellagra have been studied by Gregor, Singer, Lorenz and others. They may occur (1) independently, or (2) as a complication, of some other psychosis.

The milder degrees of mental disturbance occurring in pellagra are characterized by varying degrees of depression with or without apprehension. Such patients will speak of being "blue" or "downhearted" or fearful that something calamitous is about to happen.

In the more marked grades periods of haziness with disorientation of varying degrees develop; the lesser degrees are almost always accompanied by a feeling of fear which may be very distressing and frequently also by hallucinations.

In some cases a delirium develops more or less acutely accompanied by low mutterings, coarse muscular twitchings of the face and hands, picking at the bedclothes or irregular jerking movements of the extremities. The knee-jerks are much increased and there is resistance or rigidity manifested when passive movements are attempted. The temperature is frequently elevated and irregular. The picture then presented resembles a condition sometimes seen in delirium tremens and recalls the classical typhoid state. This syndrome, frequently terminating in death, has been described as typhoid pellagra. It closely resembles, and probably is identical with, the syndrome described by Meyer as associated with "central neuritis."

"In the instances of pellagra and an unrelated psychosis the mental picture becomes atypical. The fundamental alienation manifests itself either in all purity or is distorted by the addition of confusion or mild delirium to the already existing mental symptoms" (Lorenz). In this class of cases two groups may be recognized, one in which the unrelated psychosis was known to be present before the pellagra developed, and another in which the history of a preëxisting psychosis is unobtainable. In the former, pellagra may be considered as a complication; in the latter, the development of pellagra and the unrelated psychosis may be (1) a coincidence, or (2) the pellagra may be considered as having precipitated an insanity that was latent, or possibly (3) the seemingly unrelated psychosis really is pellagrous. Whether this last is ever actually the case cannot be stated, but if it occurs, is probably quite exceptional, for, according to Lorenz "the acute mental disturbances (confusional or delirious reactions) terminate either in recovery or in a typhoidal state shortly before death; in other words, when the patient recovers from pellagra he also recovers his mental health with very few exceptions."

(f) *Eruption*.—The disease is distinguished by a distinctive eruption which, however, fails to appear in an undetermined, but probably not inconsiderable proportion of cases in any one season. In the cases in which it occurs it develops after a period (in previously normal individuals) of not less, probably, than three or four months, during the latter portion of which more or less marked subjective symptoms have been developing. In Goldberger and Wheeler's experimental cases in adult male convicts the eruption was not observed until after a period

of not less than five months. In those who have previously had an attack, the developmental period of the recurrence may be expected to vary in proportion to the degree of the recovery preceding the return to or resumption of a faulty, pellagara-producing diet.

In some cases, particularly in children and in the insane, the symptoms prior to the appearance of the eruption may be inappreciable or very slight, or the physical deterioration may be so gradual as to escape attention, so that the eruption is or may seem to be the first recognizable indication that something is wrong. Consequently, it is sometimes necessary and often convenient, though frequently erroneous, to consider the date of the first appearance of the eruption as marking the onset of the attack of pellagra.

The eruption ordinarily begins as an erythema which may vary in intensity from a condition resembling that produced by some mild irritant, such as a mustard plaster or a superficial sunburn, to one in which there is a deep purplish redness, with or without bleb formation. In the latter event the eruption is frequently spoken of as of the wet type. Instead of a diffuse erythema, the eruption may, in very rare instances, appear at first in the form of a few irregular macules or small erythematous patches.

It is probable that in some instances the erythema is so slight or perhaps so fleeting as to escape attention, while occasionally it does not occur at all. In such event, the first thing observed is a dirty brownish point or points of pigmentation with more or less marked keratosis. The affected point or patch may extend, and from within a few days to a few weeks may, alone or by coalescence with other developing patches, come to involve a considerable area of skin.

Although at times rather evanescent, the erythema more commonly persists for several days, during which it may either become more marked or remain without appreciable change, differing in this respect from the erythemas with which it is more commonly confused. It may be active or persistent at the periphery, as a narrow red zone or areola, when the central area is already well along in desquamation.

As the erythema subsides the affected skin becomes more or less pigmented and keratosed and may take on an appearance somewhat like that of old parchment.

At this, or even at a later stage, the erythema may flare up again, involving part or all of the previously affected area and frequently also extending beyond it. This may be repeated a number of times during the same season, so that several stages of the dermatitis may be present at the same time in seemingly successive overlapping layers or strata.

The affected skin next becomes roughened by the formation of epidermal scales which, with varying rapidity, become loosened and detached. In some instances, there is not this definite scale formation; in its stead there is a mealy sort of desquamation. Less commonly the parchment-like epidermis cracks and dry flakes may rub off or be readily detached. The desquamative process generally begins at

or near the center of the affected area and progresses towards the periphery, where, by reason, apparently, of the rather abrupt emergence of the affected into the normal skin, a pigmented keratosed fringe tends to form which rather sharply delimits the involved surface and may long persist as a residual telltale of the limits of the desquamative process. The transition from involved to normal skin at all stages is characteristically abrupt, so that the pellagrous eruption tends to be sharply margined. The manner of formation and appearance of the fringe are closely simulated at the limiting margin of a blistered or desquamating area following a sharp sunburn, or the vesication following the application of a mustard plaster.



FIG. 1.—PELLAGROUS DERMATITIS ON BACK OF HAND.

Case in a native of Mexico City. Original. (Courtesy of Dr. José Mesa.)

The characters of the eruption above described are usually sufficiently distinctive to permit of recognition by the experienced observer. It possesses, however, other peculiarities which it is necessary to consider. These are its predilection for certain sites and the striking tendency to affect corresponding areas on the two sides of the body, that is, its tendency to bilateral symmetry.

Although the eruption may affect almost any part of the body surface, its favorite sites, in somewhat the following order, are: the backs of the hands, the backs of the feet, forearms, neck and face. Less frequent sites are the elbows, knees, arms and genitalia (labia in the female, scrotum and penis in the male.) Less frequently still, the palms of the hands, soles of the feet, and perianal region may be involved, and, rarely indeed, the skin over the spinal vertebræ, the scapular regions, the axillæ, popliteal surfaces, antecubital areas, the abdominal surface,

thighs and scalp may be affected. As between the flexor and the extensor aspect of the limbs, the latter is much more commonly involved. In the average case the eruption is limited to one or two sites, as for instance the backs of the hands or backs of the feet, or the backs of the hands



FIG. 2.—PELLAGROUS DERMATITIS ON HANDS AND FEET.

Margination of lesions particularly well indicated along the outer border of the right foot and a little above the left wrist. Hawaiian case in a Japanese. Original. (Courtesy, Dr. J. S. B. Pratt.)

and part of the forearms, etc. In very rare instances the eruption may involve almost all of the body surface.

On the backs of the hands, the knuckles are frequently the starting points of the eruption; from these it may extend to the backs of the phalanges of some or all of the fingers. Great variation in the extent of the involvement of these may be observed; it may extend down to and along the sides of the nails, or, and more commonly, not beyond the

proximal phalanges. More frequently the eruption extends upwards, frequently stopping just short of the wrist or it may include the latter, occasionally encircling it completely, though more commonly leaving the flexor surface partly or entirely free, thus exemplifying the peculiar tendency of the pellagrous eruption to avoid flexor surfaces. When the flexor surface of the wrist is involved, the surface affected tends to be somewhat triangular in outline, the upper limiting margin usually running obliquely from the radial border downward towards the palm or the ulnar border.

At times the eruption not only completely encircles the wrist, but may extend up the forearm, perhaps to the elbow, sometimes appearing like a glove; here, too, the rule is for a much greater extent of the extensor than the flexor surface of the forearm to be affected.

On the feet, the favorite site for the eruption to appear is at about the center of the dorsum where it may involve an area of very variable extent. At times the surface involved may extend to and involve the backs of the toes. Not infrequently the eruption involves and may be limited to the area immediately back of the outer malleolus.

On the neck the most frequent sites are at the sides, about at the center of the posterior triangle. At times the dermatitis may cover most of the upper part of the posterior triangle of each side. Although it may extend across the back of the neck, it usually does not do so, so that the lesions at the side may remain discrete patches. Another but relatively less frequent site is the episternal region. This lesion may have extensions downward on the sternum and upward and outward to the side of the neck. At times the eruption may completely encircle the neck as a band or collar (Casal's collar) of variable height. This type is relatively uncommon.

With, but more commonly without, the eruption on the face, there is at times a marked seborrhea, most frequently around the *alae nasi*, but at times involving also the chin, lips, and root of the nose or the glabellar region. The secretion is usually dry and horny in character, yellowish, and may give the affected parts a rough sandpaper-like feel.

Painful fissures may develop in the folds about the knuckles, flexures of the fingers, and palms of the hands in cases in which thickening becomes excessive. In the type of eruption with bleb formation these may become infected with danger of subsequent ulceration and healing with scar formation.

After desquamation of the lesion is completed there is left, in cases in which the dermatitis was of considerable intensity, a reddened glistening new skin which may seem somewhat thinned or may become so after repeated attacks. On the backs of the hands this condition may be rather closely simulated by senile atrophy, a not infrequent source of confusion and possible error. The livid appearance of the new skin may persist for considerable periods. In the negro one sometimes meets with a very marked residual pigmentation at the site of the dermatitis; this pigmentation may persist for months, and possibly for years after re-

covery from the attack. Caution should be exercised in interpreting actual or apparent residuals of previous lesions.

Among the most marked peculiarities of the pellagrous eruption is its notable tendency to appear about the same time and to involve similar areas both as to extent and peculiarities of outline on both sides of the body. Thus it may be stated, as the rule, that if the back of one hand or of one foot, one elbow, one knee, one side of the neck, one cheek, or the lid of one eye is affected, that the corresponding part on the other

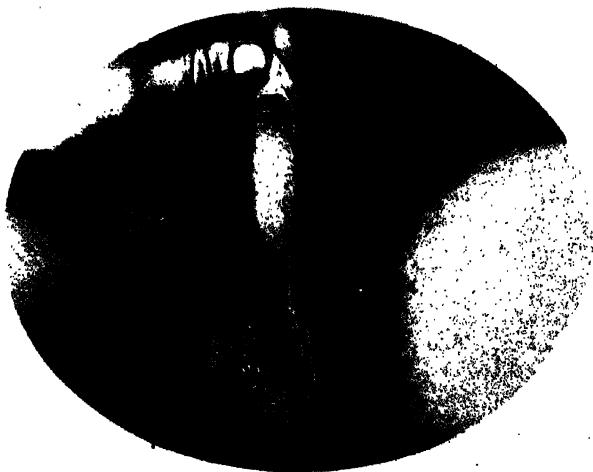


FIG. 3.—PELLAGROUS DERMATITIS ON GENITALIA.

Bilateral lesions on ventral aspect of scrotum (but not affecting the median raphe), along the median line of the under surface of the penis and the prepuce at the frenum. Experimental case. (After Goldberger and Wheeler, 1920.)

side of the body is affected, and affected to almost exactly the same extent. This rule, however, is not without many exceptions; not only may the eruption be asymmetrical, but in rare instances it may not even be bilateral, the eruption appearing only on one side, as on the back of one hand. Pellagra, therefore, cannot be excluded simply because of a marked lack of bilateral symmetry of the eruption. The pellagrous eruption ordinarily gives rise to but slight subjective manifestations. There may be a local feeling of tension with a burning or less often with a slightly itching sensation. Swelling has been described as accompanying the erythema; it is ordinarily very slight.

The seasonal appearance of the eruption has already been referred

Although it may develop at any time of the year, in the United

States in the vast majority of cases it appears in the late spring and early summer (April, May and June) and has cleared up by September or October. Thus, in an endemic locality one may search in vain for any signs of an eruption in February or March, see numerous cases in May, June and July, and again fail to find a single case after the middle of September or the first of October.

Most authorities consider that a close relation exists between sunlight and the eruption of pellagra. That exposure to the sun may accentuate the eruption need not be denied, but the evidence that has heretofore been adduced of a closer relationship does not bear critical analysis. The occurrence of the eruption (1) on covered parts, (2) in bedridden patients and (3) Neusser's observation that in naked gypsy children in Rumania the eruption affected the hands and feet, leaving the body free, just as it does in individuals who are clothed, clearly indicates that the involvement of so-called exposed parts is a specific character without necessary, if any, relation to the sun.

A diffuse general pigmentation recalling that of Addison's disease may at times be observed.

(g) *Blood*.—The blood-picture in uncomplicated cases shows no distinctive changes; at most there may be observed a slight anemia of a secondary type. The alkali reserve does not vary from the normal (Jobling and Maxwell).

(h) *Circulation*.—The blood-pressure is somewhat lowered. The pulse-rate is normal, or tends to be slightly accelerated.

(i) *Spinal Fluid*.—The cell-count is not increased (Lorenz).

(j) *Temperature*.—In uncomplicated cases the temperature as a rule is normal; occasionally one sees slight irregular elevations of short duration. In some, relatively rare, very severe cases, it may be considerably elevated and run an irregular course; this is the so-called typhoid pellagra. Typhoid pellagra may occur, however, with little or no rise in temperature, the term having reference more particularly to a neuromuscular syndrome recalling that occasionally observed in typhoid fever and delirium tremens and similar to if not identical with that described by Meyer as a central neuritis. It is not to be confused with an infection with Eberth's bacillus.

(k) *Genito-urinary*.—The menstrual function is ordinarily not disturbed, but in some instances it may be suppressed or be irregular. Menorrhagia may occur. Vulvovaginitis is a not infrequent and at times an early occurrence.

Pregnancy may go to term or in severe cases may terminate prematurely. There are reports of well-developed and well-nourished children born in the course of an attack in the mother. In four cases, however, of which the present writer has knowledge, one was stillborn, one died within a few hours after birth, and two died within less than a month; both of the latter appeared to be poorly nourished when seen shortly after birth. This very interesting phase of the subject needs further study.

In rare instances micturition may be very painful and frequent.

The urine tends to be of low specific gravity and reduced acidity; it frequently, but by no means always, contains indican; this, however, is greatly influenced by the character of the diet. Hunter, Givens and Lewis, have pointed out that a well-marked indicanuria shows a decided tendency to decline as the patient recovers from an acute attack, but if the gastric hydrochloric acid is subnormal, as it frequently is, and the diet largely animal, the indican is unlikely to return to quite the normal level.

*Pseudo-pellagra*.—The term “pseudo-pellagra” was introduced by Roussel, and has been adopted by Zeists, that is, those who believe in the corn theory, to cover a group of cases reported as pellagra without maize. Harris has recently suggested the name “parapellagra” for this group. While it is quite probable that this includes a variety of conditions having nothing to do with pellagra (instances, that is, of errors in diagnosis), it is certain that many of the so-classified cases are true pellagra, so that one is tempted to define “parapellagra” as pellagra without maize. There is now no sound reason for such terms.

**Diagnosis**.—Although the fully developed or classical picture, once seen, can hardly ever be mistaken, the recognition of the disease is not infrequently difficult because cases of the classical type form but a small proportion of the total. The eruption is the most distinctive indication of the disease and the main reliance in its recognition. It is of very great importance, therefore, to have a clear understanding of the characters which, taken together, distinguish this from other eruptions.

Great importance was at one time attached to the site of the *eruption*, it being believed that only parts exposed to sunlight were affected. The recognition as pellagrous of eruptions on covered parts has greatly reduced the significance of this point. Such significance as still attaches to it relates almost wholly to the relative frequency of involvement of different parts. It is a feature of secondary importance and should not be given too much weight. In this connection it may be well to warn against the all too common practice of limiting one's search for the eruption to the exposed skin; when a suspicion of pellagra arises no part should escape careful scrutiny.

The features especially to be considered are the pigmentation with keratosis and sharpness of delimitation of the lesion. These give the eruption its most distinguishing features. Of great importance also is the manner of its evolution; a consideration of this alone will frequently permit of a definite decision as to the nature of the eruption. Consideration must also be given to the limiting fringe. It is an extremely valuable index of a disappearing eruption; when clearly marked and bilaterally symmetrical it is in itself well-nigh pathognomonic. Bilateral symmetry is a striking but somewhat subordinate character; it helps to complete the picture but it is well to remember that the eruption may be decidedly asymmetrical and, in rare instances, unilateral.

The tendency of the eruption to recur is a feature of decidedly subordinate value in diagnosis. Judgment as to the nature of a suspicious eruption may be aided by a good history of a previous eruption, or it



may be materially aided by the subsequent appearance, during the same or the succeeding year, of a clearly marked eruption. The failure of a recurrence, however, cannot be considered as evidence against the pellagrous nature of a previous eruption.

The eruption may be simulated by chapping of the hands or feet, particularly in children, by sunburn, dermatitis venenata, eczema, and by senile atrophy with pigmentation, particularly of the backs of the hands. Careful consideration of all pertinent circumstances will usually resolve any doubts; at times it may be necessary to watch the progress and course of the eruption before forming final judgment. Rarely erythema multiforme and lupus erythematosus may simulate the eruption of pellagra to a remarkable degree. Ichthyosis has been known to cause confusion but without much reason.

In the *absence of the eruption* it is ordinarily impossible to determine the presence or absence of the disease with certainty. In endemic localities, however, a presumptive diagnosis at least may, not infrequently, be made in its absence from a careful consideration of the other *clinical manifestations*. The combination of failing strength, headache, "nervousness," vertigo, indigestion and constipation or occasional attacks of looseness of the bowels or actual diarrhea, with soreness or burning of the mouth, with or without a reddened tongue or buccal mucosa, *in the absence of apparent cause*, may be considered as very suggestive, especially if appearing in the spring. The suspicion is greatly strengthened if this syndrome occurs in a member of a household which includes a case or cases with the characteristic eruption. It is further strengthened if, after adjusting the diet of such a case by including an abundance of milk, fresh meat and green vegetables, the symptoms promptly (within about two weeks) begin to improve and then clear up without return as long as a proper diet is maintained. This therapeutic and prophylactic test must be carefully guarded and should be interpreted with caution. The suspicion of pellagra may with confidence be dismissed in one who is *known* to be and to have been a habitual milk drinker and meat eater, that is, one who habitually consumes in a mixed diet not less than a pint and a half of fresh milk and a quarter of a pound of fresh lean meat daily.

There is a very striking resemblance between *sprue* and some forms of pellagra without the eruption and differentiation may be very difficult or, temporarily at least, impossible. Marked anemia, a part of the picture of sprue, is not a feature of uncomplicated pellagra. The massive frothy stools described for sprue are unlike those ordinarily observed in pellagra; this difference, however, is not invariable, for in rare instances of pellagra sprue-like stools may occur. Whether in such cases we have the two conditions associated or not cannot be stated.

It may be worth keeping in mind that *acrodynia* presents rather marked clinical analogies to pellagra. The most suggestive difference would seem to be the predilection of the erythema of acrodynia for the palms rather than the dorsa of the hands. There is much to suggest a close kinship between the two conditions. It should likewise not be for-

gotten that *pernicious anemia* and *Addison's disease* have features in common with pellagra that may lead the unwary into error.

While there is danger that conditions not pellagrous may be diagnosed as pellagra, there is perhaps greater danger that pellagra will fail of recognition. It is important to keep in mind the possibility of pellagra in cases of "neurasthenia," "melancholia," chronic indigestion with spring exacerbations, "dysentery," "pernicious anemia," "eczema," "sunburn," epileptiform seizures, vaginitis, and obscure abdominal pains suggesting disease of ovaries, appendix or gall-bladder.

**Complications.**—A disease with such long developmental period and course as that of pellagra may of course become complicated with one of the acute infections, such as measles, influenza, typhoid fever, etc. There is nothing peculiar in this. Complications which are more directly related are (1) suppurative and ulcerative processes which may follow infections of the wet, bullous skin lesions, and (2) bed-sores in those much emaciated and exhausted. In some cases a latent tuberculosis may become active and be the cause of death. A syndrome closely resembling, if not identical with, beriberi is seen in rare instances. Edema of the lower extremities of varying degree unaccompanied by urinary or circulatory disturbance, is seen at times, more particularly in the insane; it recalls and perhaps is identical with "war edema."

**Sequelæ.**—The suppuration which may follow if infection of the bullous type of eruption takes place may lead to severe ulcerations and ultimately to unsightly scar formation. This, however, is relatively quite rare. Pigmentation of the areas affected by the dermatitis may persist for years after recovery in other respects; atrophy of the affected areas may follow a severe dermatitis, especially if repeated, and may remain as a permanent mark of a previous attack. More important are some of the nervous manifestations such as vertigo and burning of the hands or feet which may long persist, and mental alienation which may in rare instances, perhaps, be permanent. The rather common impression that the disease inevitably leads to dementia is an error that finds no support in American experience.

**Association with Other Diseases.**—A disease so highly prevalent as is pellagra in certain localities may naturally be expected to be associated with many other diseases and conditions. And this is indeed the case. It is frequently found associated with tuberculosis, with syphilis, with malaria, and with hookworm infection; in Egypt, where both the hookworm and the blood fluke are common, it is frequently associated with both these parasitic infections. It may occur in association also with amebic dysentery. The recognition of associated conditions, especially such as constitute a drain on the nutritive processes of the individual, is of great practical importance in the treatment of the case. Its occurrence in the insane has been mentioned.

*Orlèche*, a condition at the oral commissures resembling somewhat a leukoplakic mucous patch, is not infrequently found associated with pellagra in our Southern States. Stannus has described a condition re-

sembling if not identical with *perlèche* in the cases studied by him in Nyasaland, to which he attached high diagnostic value.

**Clinical Types.**—Divisions into various forms or types have been proposed by different writers. In the present state of our knowledge such are necessarily artificial to a very large degree and have little or no practical value except as they suggest that some one or other feature of the disease may be more than ordinarily conspicuous.

It is probable that the varying dominance of one or other symptom or symptoms is intimately related to as yet obscure variations in some dietary factor or factors. Goldberger and Wheeler have recently suggested that pellagra may include at least two etiologically distinct though closely related syndromes; one, the pellagra with eruption and but slight other symptoms, and the other, the pellagra with subjective and other manifestations but no eruption, the pellagra *sine pellegra*. They have suggested further that differences in initial localization of the eruption probably correspond to differences in the intimate make-up of the diet.

The disease has been observed to differ in some respects in different localities and in the same locality in different years.

**Treatment.**—**PREVENTIVE.**—As previously mentioned in the section on etiology, we do not know just what dietary factor or factors constitute the specific pellagra-producing fault. Under these circumstances, in order to assure correction of the fault and thus prevent the disease, it is necessary to add to the diet of those among whom the disease prevails as liberally as possible of the foods rich in the factors in respect to which the pellagra-producing diet may possibly be short. In other words, the indication is to provide a diet that includes in sufficient quantities and in proper form all the elements needed by the body for its healthy growth and normal activities. In order that this object may with certainty be attained, the diet should include, among other things, a sufficient quantity of milk or lean meat and a liberal supply of green vegetables and fruits, and, preferably, some of all of these classes of foods.

Milk is the most important single food in correcting the pellagra-producing dietary fault and thus in preventing pellagra, and when lean meat, green vegetables and fruit are for any reason not included in the diet or only at long intervals or in very small quantities, it is very important that at least a pint and a half of milk be taken daily. When scanty, the available milk supply should be supplemented liberally with meat and with green vegetables.

Lean meat helps in a very important degree to prevent the dietary fault giving rise to the disease, especially when but little milk is available. In such circumstances, a daily allowance of not less than 4 ounces (113.4 grams) per adult of fresh lean meat should be provided. As substitutes for part of the meat, but better as additions thereto, eggs and cheese are important. It is tentatively suggested that the diet should include a minimum of approximately 40 grams (1.4 ounces) of animal protein (milk, cheese, meat, eggs) per day. It is to be understood that only such diet is capable of preventing pellagra.

On the contrary, it is certain that diets which include but little of the animal proteins may be pellagra-preventive; unfortunately, sufficient facts are not available at present which would permit one to indicate with any degree of confidence just how such diet should be constituted.

Valuable as sources of minerals and certain vitamins are **green vegetables** (cabbage, collards, turnip greens, spinach, cauliflower, string beans) and **fruits** (oranges, grapes, apples, peaches, apricots, prunes). A generous allowance of some of these should be included in the daily diet, especially when milk is used only in small quantities. In other respects, the diet should be such as the individual is accustomed to.

With respect to the long-mooted question of the exclusion or inclusion of maize, it may be said that if the diet has been adjusted in accordance with the foregoing recommendations, **maize** calls for no special consideration, but, **as with any other cereal, may be dealt with in accordance with the individual taste or purse.** Maize is to be regarded as one of several foods which, when depended upon alone or in some special combination to furnish the principal portion of some of the essential dietary factors, may constitute a faulty, pellagra-producing diet. When supplemented, however, in the manner outlined above, this specific pellagra-producing fault is corrected, the diet becomes an adequate and wholesome one, and the disease does not occur.

**Measures looking to an increase in the supply and ready availability of milk (dairying, cow-ownership) and of fresh meat** in localities where the disease prevails are of great practical importance in the eradication of the disease. In asylums for the insane there is required also an adequate personnel to properly supervise the feeding.

**CURATIVE.—Diet.**—Having clearly grasped that in pellagra, as in beriberi and scurvy, **diet** is the primary controlling factor in the production of the disease, the clinician will readily understand that in pellagra, as in these other diseases, a **proper diet** is itself the specific treatment. With this fundamental principle clearly understood, the attention of the clinician will not be readily diverted to the pharmacopœia, which contains nothing of essential importance, so far as this disease is concerned, but will be concentrated on the **feeding.** It may confidently be affirmed that success in the treatment of the individual case will be in almost direct proportion to the attention devoted to the proper feeding of the patient.

The **diet** outlined for the purpose of prevention will serve satisfactorily in the treatment of the average case. In severe cases a **more liberal allowance of milk** should be made and **eggs** added. The **milk** should **preferably be given fresh, raw**; practically, however, it is best given in the form that most tempts the appetite of the patient. The **appetite should in all cases be most carefully conserved.** In some instances, the condition of the mouth and the sensitiveness of the stomach are such that **liquids alone** are practicable. In these **milk** should be the main reliance, with **fresh meat juice, meat broth, bean, pea or potato puree** as supplements.

Patients on **liquid diet** are frequently unintentionally starved by re-

ceiving too small a number of calories. **Food should be given at regular intervals and in prescribed quantities.** A record of consumption should be made and the intake carefully watched and maintained at as high a plane as possible. Where, for any reason, it is undesirable to augment materially the bulk, the energy intake may conveniently be increased by relatively small additions of cream and sugar. An intake of 3,000 calories per day, per adult, should be aimed at.

The diet should be increased and solid food, particularly fresh meat of some kind, given as soon as the digestive powers of the patient permit, remembering that diarrhea is in itself not a contra-indication to full feeding.

The weight of the patient should be watched. During the first week or two after feeding is begun, there may be some loss in weight, even though clinical improvement is otherwise apparent. After this, however, a steady gain may be expected; should it fail to appear, a careful scrutiny of the feeding should be made and complications sought for. Disturbing symptoms should be treated on general principles. The mouth, in cases with marked stomatitis, should be kept clean with some simple mouth wash. Diarrhea, when really severe, is practically uncontrollable by medication; in the milder forms astringent mixtures may cause a reduction in the number of bowel movements, but are liable to interfere with the appetite and so do more harm than good. On the whole, therefore diarrhea is best left alone, or rather left to the action of the diet to which it will gradually respond as it will to nothing else.

LOCAL TREATMENT.—The skin lesions only exceptionally require any attention. In the wet form, care should be taken to prevent infection. A moist, mildly antiseptic dressing will ordinarily serve this purpose. Burning of the hands or feet, when severe, may be mitigated by ice water sponges.

CLIMATOLOGY.—A change of climate is of itself not an essential in the cure of pellagra. A change from city, village or "camp" to a farm in the country or to a cooler climate has not infrequently been found to be beneficial. The benefit derived is to be attributed, however, not to the change of air as has been commonly thought, but rather to the improvement in diet that is coincidently affected. Practically all the benefits of a "change of climate" may be had at home at the cost of two quarts of milk a day.

Most cases of more than average severity do better when treated in a hospital. This is due in large part to the fact that in most homes where pellagra develops the intelligent nursing required to properly carry out the feeding is not available. Some of these cases are likely to present more or less marked eccentricities of taste with respect to the very foods (milk, meat, eggs) which it is most desired that they should eat. Such are very difficult to feed and do poorly; they call for patience tact and resourcefulness on the part of both nurse and physician.

Associated diseases and complications are, of course, to be given appropriate treatment. This is particularly important in the case of conditions that are for any reasons exhausting or such as impose a strain on

the nutrition of the individual. Thus improvement will be materially hastened if, for instance, the worms in a case with hookworm infection are expelled. It is an error, however, to assume because of the improvement frequently observed to follow, that the mere expulsion of the worms is in itself sufficient; attention to the diet is essential if the maximum benefit is to be derived and a real cure obtained.

**MEDICINAL TREATMENT.**—In the long search for a cure for this disease the *materia medica* has been freely drawn upon. The list of the remedies that have from time to time been more or less warmly recommended is thus a long and varied one. It has included **antiscorbutics**, **acids** (**vegetable and mineral**), **alkalis** (**lime water, calcium chlorid**), **diaphoretics**, **astringents**, **narcotics**, **tonics**, etc. **Quinin** was recommended over a century ago by Albera, Soler and Scudelanzoni to correct the "acrimony" of pellagra, and at about the same time Videmar went so far as to attribute to it the virtues of a specific (Lussana and Frua). Over half a century ago Landouzy recommended **quinin sulphate** and quite recently Dyer has urged **quinin hydrobromate** as being of high value. **Arsenic** has been highly considered by Lombroso and those of his school and more recently the newer preparations, such as **atoxyl**, **cacodylate of soda**, and **arsphenamin** have been tried, and, as is so characteristic of the literature of pellagra, have been praised by some and condemned by others. The explanation of the contradictory experience in relation to the value of these and other remedies is to be found in the synchronous use or non-use of a "**nutritious diet**." For, it matters little what the preparation is, so long as it is not in itself harmful, the results from its exhibition will be good if a proper diet is used at the same time, and unsatisfactory if this is neglected or not correctly observed. In a general way this was long ago recognized and emphasized, notably by Roussel: "Without dietetic measures *all remedies fail* . . . . When drugs and good food are simultaneously employed it is to the latter that the curative action belongs; the former exercises simply an adjuvant action and is without proved efficacy except against secondary changes or accidental complications." The soundness of this opinion expressed over fifty years ago has been confirmed by the results of recent studies of the writer and his associates.

There is no way at present known for determining just when the individual is cured, that is, has regained a normal state. On a proper diet the symptoms and outward manifestations may clear up in a few weeks, but it is very doubtful whether the individual has in fact completely recovered in this time. It seems highly probable that in the average uncomplicated case the normal state is not regained under three to four months of proper feeding. At the end of four to six months such individuals have been observed to react to physical strain or stress in the same way as a normal individual.

In cases complicated by some condition which acts as a drain on the nutritive processes, or in those in which the feeding is unsatisfactory, recovery may be slow and variously prolonged.

Heretofore students of the disease have conceived of a cure in rela-

tion to pellagra as such recovery as precluded the possibility of any subsequent attack or recurrence. As under ordinary circumstances, recurrences frequently take place, in some instances even after an interval of several years, nearly all authorities have heretofore taken a very pessimistic view of the treatment and eventual outcome in individual cases. But when we recall the striking analogy afforded by the tendency to recurrence observed in endemic beriberi and in endemic scurvy it is clear that the idea of actual recovery or cure in pellagra is entirely compatible with the subsequent occurrence of renewed attacks. It simply emphasizes the point that pellagra, like other diseases resulting from faulty diets, can be expected to remain "cured" only so long as a proper diet is maintained. The disappearance of symptoms or apparent clinical recovery from pellagra is not to be considered as doing away with the need for further attention to the diet. A **properly constituted diet** is at all times necessary and must be maintained if danger of the recurrence of pellagra is to be avoided.

**Prognosis.**—Earlier American experience indicated a case fatality rate of from 30 to 60 per cent. This was not, however, a true indication of the seriousness of the disease, being due, at least in large measure, to failure to recognize the milder cases. Certain it is that as familiarity with the disease has increased the impression has developed that it has become much milder. Whether this apparently diminished virulence is to be explained as entirely the result of the recognition of a larger proportion of the many mild cases cannot be stated. The reduced fatality rate is probably in part due to a better appreciation of the vital importance of diet in treatment. Reports from Mississippi show a case fatality rate averaging ten per cent. for the three years 1914, 1915, and 1916. Although the morbidity records of this disease probably include many duplicate reports, it is not believed that this compensates fully for the very large proportion of all cases that do not ordinarily come to the attention of any physician, so that as the mortality reports are fairly complete, these statistics would seem to indicate that the actual case fatality rate does not exceed, and is probably very much less than the indicated ten per cent.

In individual cases, if of any severity, the prognosis should always be guarded, for we have no satisfactory means of judging of the degree of damage sustained. While death is usually from exhaustion, or is due to an intercurrent infection, in rare instances death may be sudden, with little warning and without apparent cause, probably as the result of central nervous damage. Indications of gravity are (1) persistent vomiting, (2) diarrhea with frequent watery evacuations, and (3) marked symptoms of central nervous involvement (typhoid pellagra, central neuritis). The wet form or a very extensive eruption is generally a mark of severity; the converse, however, does not hold good. Favorable indications are a good food intake and gain in weight.

Prognosis with respect to recurrence hinges entirely on the ability and willingness of the individual to maintain at all times a proper diet. The old saying "once a pellagrin always a pellagrin" is essentially

false; it is true only in so far as it indicates that the conditions which operate to make the diet of the individual faulty do not readily undergo favorable alteration. This becomes apparent when it is realized how intimately the character of the diet may be and frequently is bound up with economic conditions, habit, and custom, and how difficult it may be to influence these favorably in individual cases.

**Pathology.**—Just how the diet operates to bring about the changes responsible for the manifestations of the disease remains for future study to determine. In the present state of our knowledge the pathogenesis of the disease is purely speculative.

Studies of the morbid anatomy, particularly of the nervous system, have been made by a number of workers, among whom may be mentioned Lombroso, Babes and Sion, Tuczek, Kozowsky, Mott, Anderson and Spiller, Singer and Pollock, and Sundwall. As cases ordinarily coming to autopsy are very commonly associated with other conditions, it is difficult to differentiate the lesions due to the associated condition from those possibly due to pellagra.

There is usually but not always marked general emaciation. The organs may be somewhat diminished in size and the musculature of the stomach and intestines may show atrophy with consequent thinning of the walls. Hyperemia with some ulceration of the mucosa may occur in the lower part of the small intestine and in the colon. The spinal cord has been found with degenerated fibers throughout the white matter; sclerotic changes have been described, however, as particularly marked in the crossed pyramidal tracts, the columns of Goll, the direct cerebellar and Gowers' tracts. Varying degrees of chromatolysis of the posterior spinal ganglion cells, of the cells of the anterior horn and notably of those of Clarke's column have been recorded. The Betz cells of the cortex and the cells of Purkinje have been observed with similar changes, particularly marked in the former. The Nissel granule cells show a partial or complete disappearance or displacement of the granules. There are usually no indications of either vascular or meningeal inflammatory changes for which the disease can be held accountable. The regressive changes are such as might be due to an intoxication or to malnutrition. Apart from the presence of the characteristic skin lesions, pellagra is not capable of recognition post mortem (Singer and Pollock).

**History.**—The first description of the disease is generally credited to Gaspar Casal, physician to Philip V. of Spain, who, in 1735, in the neighborhood of Oviedo in the principality of the Asturias, first observed some cases of what he regarded as a peculiar form of leprosy which was known to the people of the locality as "mal de la rosa." These observations were not published until 1762, about three years after Casal's death. Some knowledge of them was made known, however, in 1755, by Thieri, a French physician, who, in the course of a visit to Madrid, learned of the disease, he states, from Casal himself.

Nine years after the posthumous publication of Casal's observations, we have the first report of the disease in Italy, in a memoir by Francesco



Frapolli, of Milan (1771). Here we have for the first time in the literature, the name by which it is known at the present day—pellagra.\*

Within a few years after Frapolli's publication it was found that this disease was widely prevalent in northern Italy. This led to the establishment in 1784, at Legnano, of the first special hospital for its study. It was here that Gaetano Strambio (Sr.), who was put in charge, made his famous studies.

Outside of Italy and Spain pellagra was not heard of until 1829, when Hameau reported his observations made in the vicinity of Teste de Buche, Department of the Gironde, in the southwest of France. In 1874 there is mention by Pruner-Bey of the existence of the disease in Cairo, Egypt, and in 1858 we learn through Theodori of its presence in Rumania.

It is of interest to note that the relation of the "mal de la rosa" of Casal to the "pelagra" of Frapolli was long in dispute. It was not until 1849 that their identity was established by the investigations of Roussel. Although, as we see, the endemic prevalence of pellagra has long been known in Europe, definite knowledge of its endemic occurrence in the western hemisphere dates only from 1896 when Vales published his thesis on pellagra in Yucatan, Mexico. It is of interest to note, however, that three years before this Bowen, under the name of *psilosis pigmentosa* described as prevalent in Barbadoes what he believed to be either a new disease or one closely allied to Thin's "*psilosis linguae et intestini*" (i.e., Sprue) but which is to be recognized as pellagra. These reports of the endemic prevalence of the disease in the New World were antedated by a few reports of sporadic cases, the earliest of which was that reported by Gray in 1864 from Utica, N. Y.

Up to 1907-1908, it was believed that pellagra did not occur as an endemic in the United States. Early in July, 1907, there was reported by Geo. H. Searcy an epidemic of 88 cases, which had occurred at the Mt. Vernon (Ala.) Insane Hospital in the late summer and early fall of 1906. Shortly after this a case was reported by F. C. Merril from Texas and late in the same year J. W. Babcock recognized the disease at the State Hospital for the Insane at Columbia, S. C., publishing his observations early in 1908. From this on, the disease began to be recognized in a rapidly increasing number of localities. Within a year the disease was reported from 13 states and by the end of 1909 this number of states was doubled.

Pellagra has now been reported from all of the states of the Union but is especially prevalent in the region south of the Potomac and Ohio rivers. Credit for identifying the American disease with the disease as it occurs in Italy is due to J. W. Babcock of Columbia, S. C.

Although only a very few sporadic cases were recognized in the United States prior to 1907-1908, there is reason to believe that the disease has prevailed in a higher degree and for a much longer period than was at first thought. Babcock believes that it occurred in the South Carolina State Hospital as far back as 1828. Just how prevalent

\* Frapolli spelled it with but a single "l": "pelagra."

it was prior to 1908-1909 it is impossible to state, but it is perhaps important to recognize that it may have prevailed to quite a considerable degree without definite recognition.

**Distribution.**—Pellagra has been reported from nearly every country of Europe, from northern, central and South Africa, from India, Straits Settlements, Japan, Australia, Hawaii, some parts of South America, Panama, Central America, Mexico, the United States, Canada and the West Indies. Detailed information relating to its distribution and prevalence is, however, very incomplete. Such information as is available shows that its incidence is very uneven, both as respects different countries and different parts of the same country. Thus, northern European countries are seemingly but slightly if at all affected, while Italy and Rumania have suffered severely. With respect to Italy, it is the northern part that has been scourged, southern Italy being relatively free. Similarly, the disease appears very much more prevalent in lower than in Upper Egypt. In the United States the southern states are very much more seriously affected than the northern and western parts of the country. Furthermore, even within these states the incidence of the disease varies widely in different localities, and, interestingly enough, of two adjoining communities, the disease may be highly prevalent in one, and be almost entirely absent from the other, and this for not one season alone, but for periods of years. This phenomenon has been observed in other countries. A strikingly similar one has been reported for beriberi and for endemic scurvy.

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## SECTION XIV: DISEASES OF THE NERVOUS SYSTEM

### INTRODUCTION

It is necessary to give a brief explanation of the plan followed in the preparation of the articles on nervous diseases.

Though the general plan adopted for this work has been strictly adhered to in this section, the subject of nervous diseases requires that especial emphasis be put on several points to be mentioned.

For a long time neurology has been the bugbear of medical student and practitioner alike, when in reality its study is most fascinating. The remark is often made by physicians of intelligence: "I am a general practitioner and treat everything, but I draw the line at nervous diseases; I heartily dislike your specialty." The reason for such an attitude is not far to seek: Neurology has never been presented to them in an interesting way, and they have learned just enough to appreciate the difficulties. From the beginning it was the aim of every contributor to this section to present his subject in an easy and interesting style, a style especially suited to the needs of general practice. Clarity of presentation, therefore, was the first point required of contributors. Another and very important point for the practitioner is the need of special emphasis on symptomatology and diagnosis. Whenever possible, therefore, brief case histories have been interspersed, so as to facilitate the comprehension of theoretical descriptions. It is hoped that such case-histories will be found helpful and in some measure take the place of actual clinical demonstration of patients. And, finally, it was demanded that a fuller discussion be given to *treatment* than has hitherto been accorded to the subject in books on nervous diseases. We should never forget that patients visit their physicians to be treated, not merely to be diagnosed.

For the satisfactory manner in which the contributors have performed their assigned task the Advisory Editor on Neurology expresses his thanks.

JULIUS GRINKER, M. D.



## CHAPTER I

### INJURIES AND DISEASES OF THE PERIPHERAL NERVES

BY CHARLES METCALFE BYRNES, M.D.

Injuries of the peripheral nerves, p. 237:—Anatomy, p. 237; The process of degeneration, p. 238; The process of regeneration, p. 240; Etiology, p. 242:—Nerve lesions resulting from injury, p. 242—Symptomatology, p. 244:—Symptoms of nerve injury, p. 244; History of injury, p. 245; General examination, p. 246:—Clinical features of complete nerve lesions, p. 248:—Motor symptoms, p. 248; Sensory symptoms, p. 252; Trophic and vasomotor symptoms, p. 254:—Clinical features of incomplete nerve lesions, p. 255; Causalgia, p. 255:—Treatment of causalgia, p. 257—Clinical evidences of nerve regeneration, p. 259—Treatment, p. 261:—General treatment of nerve injuries, p. 261; Indications and contra-indications for surgical intervention, p. 261; Choice of operative method, p. 262; Postoperative treatment, p. 265:—Prognosis, p. 265.

Diseases of the peripheral nerves, p. 267:—Neuritis, p. 267:—Definition, p. 267; Etiology, p. 268; Symptomatology, p. 269; Diagnosis, p. 271; Treatment, p. 272; Prognosis, p. 274; Pathology, p. 274.

Neuralgia, p. 275.

Tumor of nerves, p. 276.

Herpes zoster, p. 278:—Definition, p. 278; Etiology, p. 278; Symptomatology, p. 280; Treatment, p. 281; Prognosis, p. 281; Pathology, p. 281.

Bibliography, p. 283.

### INJURIES OF THE PERIPHERAL NERVES

**Anatomy.**—The peripheral nervous system, with the exception of the cranial nerves and the sympathetic system, consists of thirty-one pairs of spinal nerves arranged almost symmetrically on the two sides of the vertebral column. Ordinarily, each nerve is attached to the spinal cord by a dorsal and a ventral root which unite within the intervertebral foramen to form the nerve trunk. The dorsal root presents a slight enlargement near the foramen, known as the spinal root ganglion, in which are situated the nerve-cells whose axons convey sensory impressions from the periphery to the central nervous system. The anterior root is composed chiefly of axons arising from the anterior horn cells of the spinal cord, and transmits motor impulses to the voluntary muscles. The peripheral nerves are thus composed of at least two kinds of fibres; and, with the exception of certain cranial nerves, and occasionally the first cervical nerve, all of them are of this "mixed" type. Many of them contain, also, vasomotor and secretory fibres to the blood-vessels and glandular structures, and are also said to exert a so-called trophic influence upon the tissues to which they are distributed. The existence of specific trophic fibres has, however, been questioned.

The spinal nerves are conveniently arranged into groups according to the level of the spinal cord to which they are attached; so that there

are on each side of the vertebral column eight cervical, twelve thoracic, five lumbar, five sacral, and one coccygeal nerve. After making its exit from the vertebral canal the nerve divides into an anterior and a posterior primary division. The posterior rami innervate, in general, the muscles and skin of the back, while the anterior rami unite in the cervical, lumbosacral and coccygeal region to form the various plexuses of the neck, the upper and lower extremities. The anterior divisions of the thoracic nerves usually remain ununited and proceed toward the median line of the abdominal wall as the intercostal nerves.

If a transverse section of a mixed peripheral nerve—such as the median or ulnar—is examined microscopically, it will be seen that the nerve trunk is surrounded by a connective-tissue sheath—the epineurium—which contains fat, blood-vessels, and the minute *nervi nervorum*. The nerve is further divided into bundles of fibres or funiculi, surrounded also by a connective tissue sheath—the perineurium—, septa from which ramify in the interior of the funiculi and surround the individual nerve fibres as the endoneurium.

A peripheral nerve is composed largely of medullated fibres which contain, within the center, an axis-cylinder surrounded by a myelin sheath. The axis-cylinder is always the process of a nerve-cell and is itself divided into ultimate fibrillæ. Both of these structures are enclosed in the uninterrupted nucleated sheath of Schwann. At regular intervals the myelin sheath is greatly diminished or apparently absent, while the axis-cylinder continues uninterruptedly from its cell of origin to its peripheral termination. These interrupted areas are known as nodes of Ranvier, and that portion of the nerve fibre between two nodes, consisting of axis-cylinder, myelin, and the nucleated sheath of Schwann, has been regarded by some investigators as a distinct cellular unit.

Military engagements of the World War have furnished an abundance of material for the study of problems concerning the anatomy, physiology, degeneration, regeneration, clinical manifestation, and treatment of disorders resulting from injury of the peripheral nerves. From such studies and the added impetus they have given to experimental investigation in lower animals, much valuable information has been contributed to the knowledge of nerve lesions. Many of these problems remain, however, undetermined; and conflicting opinions, together with the brief period through which some of the observations have been made, add to the difficulty of making a final decision at the present time. The neurological literature of the War has been freely consulted, and an effort has been made to incorporate in the following pages only the more significant results of these studies.

**The Process of Degeneration.**—The fundamental working hypothesis in neurology rests upon what is known as the neuron doctrine, promulgated by Waldeyer in 1891. According to this doctrine the nervous system is composed of a number of independent anatomical units, or neurons. Each neuron consists of a nerve-cell and all its processes, and the relation between neurons is by contact only. When, therefore, any part of the neuron—and particularly the axis-cylinder—is separated

from its parent cell, that portion peripheral to the lesion ceases to function and undergoes what is known as wallerian degeneration. In a complete transverse lesion of a peripheral nerve, then, according to this doctrine, the axis-cylinders of many neurons are interrupted, and it can be demonstrated that following such an injury, that portion of the nerve below the lesion not only loses its physiological properties, but exhibits the histological changes distinctive of wallerian degeneration.

When, for example, a clean incision is made of a peripheral nerve, Marie has shown that the two ends retract for a short distance, become swollen and edematous, and subsequently rounded, firm, or even distorted. Both of these enlargements are sometimes spoken of as a neuroma, although the proximal stump only consists of true nervous tissue. The distal end owes its enlargement to a proliferation of the nuclei in the sheath of Schwann, the formation of cicatricial tissue, and an increase in neuroglia elements; and, according to Nageotte, is of the nature of a true glioma. In accidental injuries, however, the two ends of the severed nerve may be connected by a fibrous strand of non-nervous material, or they may be separated by a dense scar which interferes seriously with the process of regeneration.

While these gross changes are taking place, the internal structure of the nerve is undergoing a degenerative process in both its proximal and distal portions. Three or four days after section the entire nerve peripheral to the lesion—and particularly that portion at the site of the lesion—shows dissociation of its axis-cylinders and beginning segmentation of the myelin; so that the latter stains poorly with the usual dyes, or, by the Marchi method, appears as fine black droplets. These changes are said to occur simultaneously throughout the distal portion, and are thought to originate about the internodal nuclei. The sheath of the individual fibres thus becomes swollen and distorted or, in places, collapsed from the absorption of debris. The cause of these changes and the manner in which the myelin is absorbed are still disputed questions. Kirk is of the opinion that the accompanying hyperplasia of the sheath cells has something to do with the disposal of debris as well as with the process of regeneration. Unless regenerative efforts are successfully accomplished the entire distal portion of the nerve finally degenerates into a mere fibrous band represented by the remnants of the sheath of Schwann. Changes similar to these occur also in the central stump for a distance of about one centimeter from the point of injury, and it has been maintained that the entire proximal portion of the nerve, as well as the cells from which the axons originate, share in these disintegrative changes. True degeneration in the central portion is, however, confined to the immediate region of the injury.

Those who regard the internodal segment as a cytological unit look upon the changes which have been described as a cellular retrograde process rather than true wallerian degeneration. According to this conception, each internodal segment of the nerve fibre is said to be an individual cell, composed of a vital element consisting of the nucleus and cytoplasm, and a differentiating substance which gives to the cell its



peculiar characteristics, while the axis-cylinder is in reality not a part of this unit, but a process of the nerve-cell which has to do with the preservation of neuroblastic integrity and the transmission of the nerve impulses. The nature of the neuroblastic segment is not known, but it is supposed to be nervous matter, and is said to transmit impulses before it is directly excitable.

The advocates of this doctrine claim that when a nerve fibre is sectioned the axon ceases to function, and the neuroblastic cell, deprived of this influence, undergoes retrograde changes in its differentiated substance. The whole process is comparable to the changes occurring in a muscle-cell which has been deprived of its nerve impulse. The neurilemma, like the sarcolemma, undergoes a hyperplastic change with proliferation of nuclei; the differentiated substance in each disintegrates; and these changes are said to be regressive rather than degenerative in character. True degeneration occurs only when the vital elements of the cell undergo dissolution. Mairer, in a recent article, speaks well of this segmental neuroblastic conception of the nerve-fibre and refers to its growing popularity. For a more detailed account of the process of degeneration, reference may be made to the writings of Weir Mitchell, Ranvier, Ballance and Stewart, and the later publications of Sicard, Marie, Dejerine and Tinel.

**The Process of Regeneration.**—The recovery of a nerve is of great practical interest to both the physician and the patient, and it is highly desirable that the former become acquainted with the histological changes in, and the conditions most favorable to, the healing of injured nerves.

In the study of the degenerating nerve it was stated that the proliferating cells of the sheath of Schwann probably had something to do with the disposal of the axis-cylinder and myelin debris. This hyperplasia of the sheath cells continues by mitosis; the cytoplasm increases; the cells become elongated; and thus, a protoplasmic nuclear material is formed in bands, which occupies the old sheath spaces as embryonic fibres. Since the sheath cells are concerned in both processes it is quite impossible to determine the exact stage in which regressive changes cease and regenerative changes begin.

The degenerated portion of the central stump undergoes similar changes; but unlike the peripheral portion, proceeds to complete recovery with overproduction and irregular outgrowth of new fibres. Unless, however, the two ends of the severed nerve are united under suitable conditions, the distal portion never progresses beyond this embryonic state, and finally disintegrates entirely. In the recent monograph by Purves Stewart and Arthur Evans the position is still maintained that regeneration proceeds from both the proximal and distal ends. Many unsuccessful attempts have been made to demonstrate the autogenous regeneration of nerves; and it is true that in some instances regeneration has been successfully accomplished *in vitro*, but only when the excised material has contained nerve-cells. It was also found that the experiment was unsuccessful, and that the sheath cells showed no vital reaction unless, before making the transfer, sufficient time had been

allowed for peripheral degeneration. The opinion was at one time entertained that a more rapid recovery of the severed nerve and the prevention of secondary degeneration might be secured if the two ends were immediately sutured; and Harrison's brilliant experiments upon frog larvæ, in which it was found that early union of the severed portions was followed by recovery without preceding degeneration, encouraged this belief. It seems, however, from the studies of Howell and Huber and the recent clinical observation during the War, that in the adult, at least, the peripheral portion inevitably degenerates throughout its entire extent, even to the muscle end-plate. Huber and his associates, in a series of later experiments, have concluded that regeneration always proceeds from the proximal stump; that the peripheral portion takes no active part in the process; and that regeneration does not occur without the formation of protoplasmic bands.

In order, then, for regeneration to proceed further than the embryonic state, suitable union must be established between the severed ends, since it is generally taught that the central stump exerts a so-called biochemical or trophic influence over the peripheral end and that, unless the conditions favorable to neurotropism exist, complete regeneration does not occur. With the beginning regeneration an outgrowth of axis-cylinders from the central stump occurs about the second week and proceeds at the rate of from 1 to 1.5 mm. a day; but according to Tinel, the growth may be as rapid as 3 mm. a day in the young, and varies considerably in different nerves. As the peripheral stump thus becomes sensitized by the central connection and the invasion of newly formed axis-cylinders, the sheath nuclei, according to Mairêt, increase in number and approach the periphery of the membrane. Newly formed myelin then begins to appear at about the fifth week and is, in Kirk's opinion, a down-growth from the central stump; although in the opinion of others it is still thought that the myelin may be a secretory product of the sheath cells. In the experiments of Howell and Huber, regeneration was not complete until the eleventh week after suture, although return of irritability was observed as early as the twenty-first day. It was also observed that the irritability of the nerve was greatest at the point of suture and that it decreased as the periphery was approached. Return of sensory irritability was found to occur earlier than motor irritability. During the process of regeneration there is an overproduction of axons in the proximal stump, and straying of both the sensory and motor fibres takes place; so that it is not uncommon to find the new nerve with its architecture much disarranged. This rearrangement of the "nerve pattern" has been the subject of careful inquiry during the recent War, and has offered an explanation for some of the vicarious clinical results observed in the regeneration of nerves.

Regeneration following actual loss of nerve substance has been studied experimentally by Kirk and Lewis. After resectioning from 1 to 3 cm. of a peripheral nerve the two ends were left separated but enclosed in a sheath of fascia lata, and the process of regeneration and bridging of the gap observed during different stages. During the first

two or three days abortive regenerative changes occur in both ends of the severed nerve, and particularly about the central stump. The fascial tube about the fifth day is filled with a secretion resembling brain material which is the product of the severed ends and not of the fascial covering. In the earlier stages the nuclei of the sheath of Schwann undergo active proliferation with the formation of protoplasmic bands. This is soon followed by disintegration of the proximal stump and degeneration throughout the entire peripheral segment. Active regeneration then begins, and protoplasmic bands are formed which appear to invade the exudate within the fascial sheath, from both ends of the severed nerve, but more rapidly from the central end. These bands sometimes anastomose or are diverted by the invasion of scar tissue and thus lead to a deflection of the axis-cylinder with disorganization of the nerve pattern. It is thought that the protoplasmic bands direct the course of the newly formed axis-cylinders as they invade the peripheral portion, and that a down-growth of axons does not occur without the previous formation of the nuclear bands. Clark's studies upon *beriberi*, where degeneration and regeneration are said to be subject to control, appear to contradict this belief. He observed that if degeneration were stopped before a reaction occurred in the sheath cells the fibre bands were not formed; and that the axis-cylinders were always a down-growth from the central stump, and invaded the peripheral nerve even in the absence of protoplasmic bands.

**Etiology.**—NERVE LESIONS RESULTING FROM INJURY.—The frequency, character, and consequence of nerve injury vary widely in civilian and in active military life, and according to the anatomical protection the individual nerves enjoy. The causes of nerve injury are numerous. In civil life, fractures, dislocations, pressure from abnormal positions during sleep, from the use of crutches, from bandages, and the pursuit of certain occupations are occasionally complicated by an associated nerve disorder. Stab wounds, injuries from broken glass, and stretching or tearing of a nerve from excessive muscular exertion are occasionally encountered during the peaceful pursuit of general practice. Paralysis from faulty positions during prolonged ether narcosis and obstetrical palsies are more or less familiar disorders. Dyke has recorded an instance of peripheral nerve injury following the injection of antitetanic serum, and the author has seen paralysis of the ulnar nerve from the careless injection of antityphoid serum into the nerve-trunk. Nevertheless the percentage of nerve injuries in civil life is comparatively small, and most of the knowledge concerning lesions of the peripheral nerves has been derived from the studies of Wier Mitchell during the Civil War, from the experimental studies of Ballance and Stewart, Huber and his associates, and from the abundance of material furnished by the recent World War.

It was found during the World War that the percentage of nerve injuries varied slightly in the field and in the base hospitals. Sir Berkley Moynihan is of the opinion that primary injury of the peripheral nerves is comparatively rare on the fighting line; but because of

the nature of the wounds, the subsequent formation of scar tissue and the frequency of wound infection, nerve lesions are not an uncommon complication and form a large percentage of injuries recorded in the base hospitals. In Souttar's statistics, primary injury to the nerves was of frequent occurrence, although the great majority of them showed a marked tendency to spontaneous recovery. Tinel, in his wide experience, has recorded a large number of primary and secondary peripheral nerve injuries in which he finds that the nerves of the upper limb are much more frequently affected than those of the lower. This opinion seems to be confirmed by the experience in most military hospitals, but space will not permit a detailed review of the statistics of individual observers or of the frequency with which individual nerves are injured. Although any of the cranial or spinal nerves may be injured during active warfare, it is remarkable how frequently the cranial, cervical and cervical sympathetic nerves have escaped.

From the statistics of Tinel, Moynihan, Price, White, Spear, Stewart and Evans, Noon, Benisty, and others, it is apparent that certain nerve plexuses, as well as the individual nerves in a given plexus, suffer more frequently than others. Thus it was the experience, in general, that of the cranial nerves, the facial was most often involved, and the spinal accessory the least frequently affected. Injury to the nerves of the upper extremity was of common occurrence, while lesions of the entire brachial plexus were comparatively rare. In lesions of the brachial plexus, the upper or outer cord of the plexus was most frequently affected. Of the individual nerves of the brachial plexus, it seems that the radial, the ulnar, and the median, in the order given, were the most common lesions, although the statistics from many Army hospitals vary considerably as to the relative frequency of radial and ulnar involvement. Injury to the nerves of the lumbar plexus was relatively uncommon and, of these, femoral lesions were most often encountered. The nerves of the sacral plexus were frequently affected and second only to injuries of the upper extremity. The sciatic nerve was most often involved, with external popliteal lesions next in frequency. Injuries of particular nerves, such as the median and sciatic, exhibited certain peculiar features which will be referred to in another section.

The more common causes of nerve injury in active military life are, in the experience of Sir Berkeley Moynihan and Byron Bramwell, due to concussion, contusion, compression by surrounding structures, inclusion in scar tissue, hemorrhage, and, in the great majority of cases, suppuration. Disturbance in the blood supply, without direct injury to the nerve, has, in a few instances, been responsible for the development of peripheral nerve symptoms. It was also observed that a missile may have only pierced the nerve-sheath, or merely separated the nerve-fibres without actually severing them, and thus led to the invasion of scar tissue, or the development of a central hematoma with subsequent fibrosis and the formation of a central false neuroma. A nerve may thus be merely bruised or suffer partial or complete destruction of its fibres. It is also significant that there may be evidences of complete

physiological interruption without actual loss of anatomical continuity, and that the individual fibres of a nerve may suffer unequally. When there are evidences of complete physiological and anatomical interruption of the nerve it has been shown, from the studies of Marie and Foix, Tinel, Moynihan, Bramwell, Dejerine, Langley, André-Thomas, Mme. Athanassio-Benisty, Babinski, and others, that one of several gross changes may be present. The ends of the severed nerve may be more or less approximated, or separated by a distance of several centimeters, and either lost in scar tissue or joined by a filament of non-nervous matter. Occasionally, when the two ends are completely separated, both become swollen and distorted with the formation of true and false neuromata. It was, for a time, believed that the formation of scar tissue had a more or less favorable influence upon the process of regeneration, but it has been suggested by Pitres that the scar tissue takes no direct part in the recovery and may even interfere with perfect regeneration. Careful inquiry should then be made into the nature of the lesions; but unfortunately, it is occasionally extremely difficult, if not impossible, to determine from the clinical or even the direct examination of a nerve the exact nature of the pathological condition.

**Symptomatology.**—**SYMPTOMS OF NERVE INJURY.**—With the exception of a few of the cranial nerves, the peripheral nervous system is composed of fibres subserving several functions, for each of the spinal nerves contains four kinds of fibres with specific conductivity. Except for the presence or absence of myelin, no anatomical distinction can be made between the different fibres, although physiologically they may be arranged in the following groups:

- (1) Efferent, or motor fibres to the striated muscles.
- (2) Efferent, vasomotor preganglionic fibres from the central nervous system to the sympathetic ganglia.
- (3) Efferent fibres from the sympathetic ganglia to the smooth muscles, glands, and vessels.
- (4) Afferent sensory fibres from the posterior root ganglia.

These groups of fibres are said to occupy a more or less fixed position within the nerve trunk, so that for certain nerves, a fairly constant architecture has been determined for the sensory and motor elements, which Langley has designated as the "nerve pattern." Dejerine had previously called attention to the probability of a radicular arrangement of fibres within the peripheral nerve, and André-Thomas has more recently described motor dissociation in peripheral nerve injuries characterized by isolated paralysis of individual muscles. Compton, from a study of the fetal and adult sciatic nerve, has concluded that the grouping of fibres is such that the trunk may be injured or even partially divided with the escape of either the motor or sensory elements; and that the levels from which these two systems of fibres leave the main trunk of the nerve are quite constant. This study of the internal structure of a nerve or the "nerve pattern" has contributed much to the knowledge of the finer anatomy of the peripheral nerves, and fairly well-defined arrangements of sensory and motor fibres have been de-

terminated for most of the larger nerve trunks, and particularly for the median and sciatic nerves.

The general symptoms of nerve injury vary, then, according to the degree of damage which the nerve has suffered, the particular portion of the nerve which has been injured and the function of the affected fibres. White has called attention to the frequency with which apparent physiological interruption is associated with unsuspected anatomical lesions, and finds this condition especially common in injuries of the cauda equina, brachial plexus and sciatic nerve. It is important, therefore, in every case of nerve injury, both as to prognosis and treatment, to determine as accurately as possible: *first*, if there is complete interruption of the nerve impulse, and if so, whether the nerve is anatomically divided or if there is mere physiological interruption of conductivity; and *second*, whether an operation is necessary, when it should be done, or whether or not the nerve will recover without operation. Ordinarily, it is not difficult to determine, clinically, the presence and degree of physiological interruption, but it is, at times, quite impossible to arrive at a definite opinion concerning the actual changes in the nerve. If an anatomical lesion is suspected it is important to know something of its nature: whether there is actual loss of nerve tissue, or whether the symptoms are due to adhesions about the nerve, to compression from surrounding tissues, to local ischemia, or to the formation of an intra-neural fibroma or hematoma.

Neurological studies during the recent War have shown the desirability, and, at the same time, the difficulty of correctly interpreting the clinical results of peripheral nerve injuries. They have also taught that not only must careful and repeated examinations be made of the motor, sensory, vasomotor and electrical changes; but that much is to be learned from a direct examination of the initial wound, the points of entrance and exit of the missile, and from palpation of the injured area. The writings of Macdonald, Dejerine, André-Thomas and Edwin Bramwell have contributed many interesting clinical refinements in diagnosis and emphasized the necessity of a thorough clinical study in each case.

**HISTORY OF INJURY.**—The interval between the infliction of the wound and the development of the paralysis is, according to Bramwell and Price, of diagnostic value. If the paralysis is not simultaneous with the injury, complete division of the nerve may be excluded. A slowly developing paralysis generally indicates the development of scar tissue or callus, while pronounced paralysis appearing sometime after the injury is said to be almost certainly functional. Bramwell also considers it important to make inquiries concerning alterations in the blood supply resulting from injuries of the arteries and veins. If the patient is not seen immediately after the injury, information as to the probable nature of the nerve lesion may be secured from a history of the character of the wound, the kind of projectile, what happened at the time of injury, and the position of the body, as well as from an examination of the entrance, exit and direction of the bullet. Careful inquiry should also be made as to the development of any superadded functional or organic symp-

toms, such as the occurrence of spasm, contracture, or paralysis. The presence or absence of sensory changes, hemorrhage, pain and vasomotor disorders, and an account of the progress of the condition following the injury are, in Price's opinion, valuable historical data.

**GENERAL EXAMINATION.**—Much importance has been attached to the local examination of the wound and the variation in symptoms experienced immediately after the injury and those which develop after the patient has been transferred to one of the Neurologic Centers. The site, location, character, degree of healing of the wound, and the presence of vasomotor and atrophic changes are of importance in determining the extent of nerve injury; although the value of the information obtained from direct observation depends somewhat upon the extent of time which elapsed between the occurrence of the injury and the examination. The infliction of a wound in which there is much destruction of tissue with extensive scarring suggests that part of the nerve-trunk was also carried away with the fleshy tissues, and that the nerve is completely divided, with perhaps a variable gap between the two ends.

Palpation of the nerve at the site of the lesion is also helpful in determining the nature of the lesion. By this means information may be obtained as to the size of the nerve-trunk, the probability of its complete division with loss of nerve substance, the presence of scar tissue, and the development of fusiform swelling of the nerve accompanying the formation of intraneural fibromata, hematmata or neuromata. Dejerine has called attention to the observation that if there is absence of pain, tingling, or irritation upon pressure over the nerve below the lesion, complete division of the nerve is most probable; but that the absence of these symptoms gives no indication as to the anatomical nature of the nerve obstruction. If, however, irradiation is elicited below the lesion, it is indicative of incomplete division of the nerve or beginning regeneration. André-Thomas finds examination of the cicatricial and pericicatricial skin surfaces of value. If sensory examination of the skin produces painful or other sensations referred to the periphery, this condition of topoparesthesia suggests an anatomical lesion of the nerve which may be complete or partial. It is worthy of note that irregular crossing of nerve-fibres may sometimes result in the projection of a sensory impression to a region innervated by a nerve other than that which has been injured.

From the most painstaking local and neurological examinations it is generally accepted that in many instances there is no positive means of determining with certainty, from the clinical features alone, whether the nerve has been completely severed or whether or not there is an insuperable barrier to recovery. This is generally true of recent injuries, and, according to Bramwell, of gunshot wounds in particular, so that further refinements in clinical methods are especially desirable.

The recognition of these diagnostic difficulties necessarily created, for a time, what Macdonald designates as an attitude of "look and see." It was maintained that no particular harm was done by exploratory incision and direct observation of the injured nerves, and that

exposure of the nerve offered the additional advantage of direct electrical stimulation. By this means the degree of conductivity could be tested above and below the lesion—an especially desirable procedure in incomplete separation of the nerve-trunk. Langley suggests that the test may be made without incision, by introducing subcutaneously a long electric needle covered with shellac, except at the point; and Bristow claims that selective stimulation of the fibres, according to the nerve pattern, may thus be practiced. The latter has also observed that, in an unexposed nerve, either voluntary motion or faradic irritability may be the first evidence of returning function; while in the exposed nerve faradic response always precedes return of voluntary motion.

The hope was also entertained that by exploratory incision definite information might be secured as to the nature of the lesion. Entanglements in scar tissue, local nerve constriction, fusiform dilatations, and the presence of neuromata could thus be directly observed and the surgeon and the neurologist be enabled to answer at once the important question of the necessity for the adoption of further surgical measures or the probability of recovery without further intervention. No doubt, in many instances, valuable information was thus obtained and, according to Bramwell, it is not uncommon to find one or more of the following pathological states: complete severance of the nerve with loss of tissue and separation of the divided ends; partially divided or nicked nerves; strangulation of the nerve by scar tissue; fusiform swellings; or attenuation of the nerve at the site of the injury with bulbous swelling of either or both ends. The nerve may be congested or healthy-looking with only a local induration upon palpation, and under these conditions a decision as to the proper course of treatment is extremely difficult if not impossible.

The not infrequent failure, then, to secure the desired information by direct exposure, and the growing belief that, in many cases, a policy of "watchful waiting" would have been more desirable, led to a general condemnation of exploratory incision in nerve injuries. Direct exposure was not only useless, but was often distinctly harmful, and Macdonald, Bramwell and others have summarized the disadvantages of direct examination in the following conclusions:

(1) Exploration often results in injury to neighboring healthy nerves and a disturbance of blood supply in the field of operation.

(2) Damage might be done to a nerve already in the process of repair; and regenerating nerves are especially susceptible to mechanical injury.

(3) Nerve fibres possess a natural tendency to recover, and this is particularly true of contused, concussed, or compressed nerves. Even completely divided nerves recover a surprising degree of function, and Souttar claims that the destruction of as much as one-third of the nerve may be followed by almost complete functional recovery.

(4) The advantage to be gained from direct electrical stimulation of a nerve is greatly overcome by the disadvantages of exploration.

(5) Recovery from secondary suture is always slow and often incomplete.

Although, in an individual instance, the interpretation of symptoms may be difficult, Noon finds, from a varied and extensive experience, that certain generalizations may be made which are helpful in arriving



at a fairly accurate conclusion as to the condition of the injured nerve. Thus, he holds the opinion that the following symptoms are of differentiating value:

Complete division of a nerve is characterized by complete motor paralysis, loss of all forms of sensibility, pallor and coldness of the affected part, diminution of subcutaneous fat, dryness and, at times, ulceration of the skin.

Nerve compression is to be suspected when, after the injury, there is a period of improvement followed by a relapse. Motor paralysis is less marked; there are no trophic changes, but there may be dissociation of sensation in which pain loss is greater than tactile loss. This type of injury he finds of frequent occurrence and feels that it offers the most favorable conditions for operative interference.

Incomplete division of the nerve with symptoms of local irritation is most probable when the motor paralysis is incomplete and associated with neuralgic pains. The skin is generally glossy, mottled, red, tender to pressure, and bathed in a profuse, strong, acid, foul-smelling sweat.

Concussion is usually accompanied by the symptoms of interruption of the nerve impulse followed by restoration of function and complete recovery within a short period. Sensory and motor loss may occur, but there is no wasting.

**THE CLINICAL FEATURES OF COMPLETE NERVE LESIONS.**—The symptoms of complete physiological interruption of the nerve impulse, if of sufficient duration, are quite constant whatever the nature of the lesion, although they vary according to the function of the injured fibres, and are therefore more conveniently discussed in terms of their physiological properties, as motor, sensory, trophic and vasomotor.

**Motor Symptoms.**—When a nerve innervating the voluntary striated musculature is completely divided there is immediate complete paralysis of both voluntary and reflex activity, and the muscle becomes flabby and atonic. The tendon-reflex is immediately abolished; in the course of ten days or two weeks certain electrical changes take place; the mechanical irritability of the muscle diminishes; and, unless restoration of function is soon established, all forms of excitability are lost. The muscle finally undergoes complete atrophy with the development of secondary contractures. It is important to know that not all of the muscles ordinarily innervated by a completely severed nerve necessarily share in the paralysis, for White has shown that it is not uncommon to find atypical muscle innervation; so that a partial muscle paralysis does not, of itself, contradict a diagnosis of complete nerve injury. As the paralysis persists and loss of tone becomes more marked, the affected part assumes a more or less characteristic position due to atony, the effect of gravity, and the overaction of unopposed muscles—a condition often seen in the familiar wrist-drop of radial palsy. But atony is not always an evidence of motor paralysis.

Under the influence of normal innervation the voluntary muscles are in a state of slight, though variable contraction; and this constant tension, known as "muscle tone" is dependent upon the integrity of the

reflex arc. If either the afferent or efferent fibres of this arc are interrupted, muscle tone suffers, but not to so great an extent from injury to the sensory fibres as from injury to the motor impulses. Loss of tone is recognized clinically by changes in the contour of the muscle, by its soft flabby consistency, the ease with which it may be stretched, the position of the affected part, and the consequent increased mobility of the joint. With the diminution or loss of tone there is also diminution or loss of the tendon-reflex, since the tendon-jerk is dependent upon both the integrity of the reflex arc and the preservation of muscle tone.

The lower motor neuron, situated in the anterior horn of the spinal cord, is said to exert a trophic influence upon the muscle cells. If a muscle is separated, then, from its spinal nerve supply, and no artificial means are adopted to maintain its nutrition or to exercise its biological property of contractibility, it undergoes regressive and atrophic changes, and may, in time, be completely replaced by connective tissue. Atrophy usually makes its appearance about the second or third week after injury to the nerve, and finally results in the development of passive contractures and deformity. The cause of muscular atrophy following a nerve or anterior horn lesion has been attributed to a disturbance in this trophic influence following the break in nerve-muscle continuity; but more recently, Stevens explains it upon a theory of fatigue from overactivity of the injured muscle fibres which are said to undergo active fibrillation following nerve section. In a series of experiments in which he sectioned the facial, hypoglossal and tibial nerves in dogs, it was observed that, from three to six days after section, incessant fibrillary activity of the muscle takes place and continues until the muscle is completely degenerated, or until there are evidences of regeneration in the nerve. Schiff at first believed that a muscle deprived of its nerves assumes a state of complete rest, but he later learned, from experimental section of the hypoglossal nerve, that automatic rhythmic contractions of individual muscle fibres develop and persist for a long period. He did not, however, associate this fibrillation with the atrophic changes. Stevens found that on the fourth day after section of the hypoglossal nerve fibrillation begins in a portion of the tongue and twenty days later involves its entire musculature. The contractions were said to be incessant and at the rate of 10 to 20 per second. In one of his experiments the animal was observed for a period of one hundred days. During this time the contractions continued, but disappeared with return of voluntary power. Atrophy, he claims, is due to fatigue from continuous fibrillation, and it has been demonstrated that the overacting muscle shows shrinkage and lowered specific gravity when compared with the normal muscle.

There have been several explanations offered for the development of contractures after nerve injury. The formation of scar tissue and the overaction of unopposed muscles were, for a time, generally accepted causes. André-Thomas is of the opinion that contracture is an irritative phenomenon dependent upon the excitation of motor or sensory fibres, errors in alignment after suture, or perhaps upon reflex sympathetic

stimulation. Spiller also has expressed a similar opinion as an explanation for the occurrence of facial spasm and permanent contracture in cases of Bell's palsy. These, he feels, are due to errors of alignment and overactivity of the abnormally innervated muscle with subsequent shortening of its fibres from excessive stimulation.

Electricity—a much abused but valuable therapeutic and diagnostic agent—is often slighted by the general practitioner either because it is thought to be too time-consuming or because it is imagined that special skill and training are required in its application. Something is, however, to be learned from an electrical examination and even the busy practitioner may acquire the principles of electro-diagnosis with comparative ease. A normal muscle responds to both the faradic and the galvanic currents when stimulated directly or through its motor nerve, and the response to both forms of current is vigorous and rapid; but the galvanic current gives a contraction only when the circuit is closed or opened. During the first week or ten days after complete division of a nerve the electrical reactions are only quantitatively altered, but later it will be found that the muscle can no longer be stimulated by either form of current when applied to the nerve; that direct faradic stimulation of the muscle produces no response; that galvanic stimulation of the muscle causes a slow, lazy contraction; and that occasionally the contraction formula is reversed, so that the anodal closing contraction is greater than the cathodal closing contraction. These electrical changes are designated as a reaction of degeneration, and abbreviated as R. D. or E. R. Unless the nerve regenerates, the muscle, in time, undergoes complete degeneration and loses all forms of electrical excitability. An electrical examination should be made of all accessible portions of the nerve, for it has been found that the conductivity of the nerve varies when it is stimulated above and below the lesion. Thus, a lesion within a nerve may block the impulse so that a stimulus from above fails to produce a response, although that portion of the nerve below the lesion retains its conductivity; or sometimes the regenerating portion of a nerve is inexcitable to direct stimulation, while a stimulus from above the lesion causes a distinct muscle contraction.

Unfortunately, the electrical reactions obtained from direct stimulation of the muscle give no indication of the nature or severity of the nerve lesion, for it has been demonstrated in the studies of Adrian that in perineural or neuritic irritation voluntary power may be retained in a muscle in which there is atrophy and reaction of degeneration; that the reaction of degeneration may be obtained in incomplete nerve division; and that even after complete nerve division the muscle response may be normal. Moynihan and White have confirmed these observations and expressed the further opinion that the polar changes in the galvanic reaction are of little value, although it has been generally taught that reversal of the contraction formula is an essential feature of the reaction of degeneration. The author's experience in the Johns Hopkins Hospital Dispensary has confirmed this more recent opinion and convinced him that reversal of the contraction formula is the last

important element in the reaction of degeneration. It was frequently found unchanged in muscles which exhibited all the other features of the reaction of degeneration, and in one instance of left facial paralysis the normal formula was preserved upon the affected side with complete reversal of the formula upon the healthy side.

It has become rather generally accepted, then, that, although little definite information is to be secured from an electrical examination alone, it is, in conjunction with other clinical methods, a useful form of investigation. In all probability the deficiencies of the usual methods of electrical examination were due to the need of further refinement in the construction of electrical apparatus, and it was found that more accurate information could be secured by the "condenser testing" of paretic muscles. The method was first used by Dr. Lewis Jones and has been successfully employed by Hernaman-Johnson who records the use of the method over a period of three years. As an instrument of precision he finds it especially valuable, and is of the opinion that by this means he is enabled to determine the degree of injury to the nerve and whether it is in a process of regeneration or will regenerate without surgical intervention. He describes the technic fully and claims that the method furnishes an accurate means of measuring the current strength and controlling the duration, length of impulse, voltage, and rate at which successive impulses are discharged. A standard scale of condensers is used, according to the table devised by Dr. Jones. The duration of the discharge varies from  $1/24,000$  to  $1/200$  of a second, and the length of impulse from the faradic coil varies from  $1/600$  to  $1/12,000$  of a second. Sir Berkeley Moynihan has, however, found the method of little clinical value. Bourguignou, with condensers of known capacity, has used the method for determining the velocity of muscular excitability and finds that it furnishes some evidence of the degree of nerve degeneration. He obtains the minimum duration of a galvanic current of minimum intensity necessary to cause a muscle contraction. The threshold stimulus of a current of indefinite duration is first determined and this is termed the "rheobase." A current of twice this intensity is then employed and its minimum duration is determined as the "chronaxie."

Direct mechanical excitability of the muscle, though often neglected, is, according to Bramwell, Dejerine and others, of diagnostic value. Bramwell states that if a muscle responds to faradic stimulation it responds sharply to mechanical irritation, and that when faradic irritability is lost the mechanical response diminishes and finally disappears entirely with the loss of galvanic irritability. Other motor phenomena observed in paretic muscles are probably of an irritative nature and are characterized by spasm and fibrillation, but are said to be rarely observed in complete nerve lesions. Spasm, when present after complete nerve destruction, has usually been explained as a reflex irritative sensory phenomenon, while fibrillation is thought to be due to direct irritation of the muscle fibres. Certain reflex types of paralysis described by Labinski, Froment, and others are regarded as probably functional

in origin, but not psychogenic, although most American neurologists regard them as of a purely psychic nature.

*Sensory Symptoms.*—The sensory disturbances following injury or disease of a peripheral nerve vary according to the nature and location of the lesion. An irritative or partial lesion of a nerve is usually accompanied by subjective disturbances of sensation manifested as pain, paresthesia and local vasomotor and trophic disorders, with occasionally a minor degree of sensory loss. It might be generally supposed that complete severance of a nerve is followed by a total loss of sensation in the cutaneous area to which it is distributed, but although there is a definite objective loss of sensation, not all forms of sensibility are equally involved, nor does the anesthetic area correspond exactly to the anatomical distribution of the injured nerve. The sensory loss is always slightly less extensive than the skin surface to which the nerve filaments are distributed, and this restriction of the anesthetic field was explained by "overlap" of the adjoining healthy nerve filaments. The painstaking studies of Head, Head and Rivers, Head and Sherren, and Thompson and Trotter have, up to the present time, occupied an important position in the clinical examination of sensory disorders following nerve lesions. Head and his colleagues, Sir James Purves Stewart and Evans are of the opinion that the afferent fibres of a peripheral nerve may be divided into three systems conveying epicritic, protopathic and deep sensibility.

The epicritic or determining fibres are said to convey light touch, minor degrees of temperature ( $20^{\circ}$  to  $40^{\circ}$  C. [ $68^{\circ}$  to  $104^{\circ}$  F.]), designated as "warm" and "cool," localization of tactile impressions, and the two-point contact, or discrimination sense. Protopathic sensibility or primary sensations include all cutaneous pain and the greater degrees of temperature, below  $20^{\circ}$  C. and above  $40^{\circ}$  C., known as "hot" and "cold." The superficial cutaneous nerves are thought to convey only epicritic and protopathic sensations. The third system of fibres which have to do with deep sensibility conveys the sense of pressure, and muscle, tendon, joint, and vibration sensations arising from the deeper structures. Bramwell calls attention to the fact that in testing these various types of sensation due regard must be had for individual variations within normal limits. It is also important to observe the level of the nerve lesion, and to make careful comparison of the affected area with a known standard for the particular nerve involved. If, then, a purely cutaneous branch alone is sectioned, deep sensibility, according to this doctrine, should not be affected, but it does not necessarily follow that deep sensibility is completely lost even in a high section of the nerve in which the muscular branches are involved, for it has been shown that fibres conveying deep sensibility undergo frequent anastomoses and may enter the deeper structures some distance from the periphery of the extremity.

Price is of the opinion that the examination of touch and pain alone is of sufficient clinical service, and Cobb claims that the variations in sense qualities depend upon qualitative difference and quantitative un-

equivalents, and that clinical examinations should accordingly be simplified by the use of quantitatively standardized stimuli. Byrne has questioned the value of Head's studies and classifies sensation into "affective" and "critical" systems. These are further subdivided into "superficial critical" consisting of light touch, nearly neutral temperatures and the light contact of compass points, while "superficial affective" sensibility consists of pain from a moderate pin-prick, cold ( $0^{\circ}$  to  $22^{\circ}$  C. [ $32^{\circ}$  to  $71.6^{\circ}$  F.]) and heat ( $40^{\circ}$  to  $55^{\circ}$  C. [ $104^{\circ}$  to  $131^{\circ}$  F.]). Pressure sense, localization, posture, passive movements, and the recognition of size, shape, and weight are classified as "deep critical" sensations. The "deep affective" sensibilities consist of pressure pain, and the extreme degrees of temperature ( $0^{\circ}$  to  $55^{\circ}$  C. [ $32^{\circ}$  to  $131^{\circ}$  F.]) in massive prolonged application. The critical system is said to preside over the affective system, and disturbance of the two systems in disease results in an overflow of neural energy brainward, with the development of spontaneous pain and pathological tenderness. Affective sensibility is placed in the thalamus, and critical sensibility, according to Bryne, is a function of the cerebral cortex.

Dejerine and Muzon, from a study of war injuries, have concluded that the absence of pain upon pressure over the nerve trunk below the lesion and the complete absence of pain when the paralyzed muscle is pinched are evidences of complete division of the nerve.

The vibratory sense, or so-called osseous sensibility, was first studied in 1889 by Rumf and continued later by Max Egger, Williamson and others. The examination is ordinarily made by means of a vibrating tuning-fork with a low rate of vibration varying from 13 to 1,000 per second. The foot of the fork is then placed over certain bony prominences, such as the styloid process of the ulnar, the sternum, the sacrum, or the anterior tibial surface. Exact methods of estimating the duration of the vibrations experienced by the patient and the corresponding difficulty of determining a normal standard of duration have, up to the present time, been the principal defects in estimating the vibratory sense. Symns claims to have overcome these difficulties by using a fork with a window so placed that the amplitude of the vibrations may be observed. Besides various forms of neuritis, Symns studied the vibratory sense in nine cases of nerve injury and arrived at the following conclusions:

Diminution of the vibratory sense is not necessarily associated with loss or disturbance of other forms of sensibility.

Return of vibratory sense may be later than the return of other sense qualities.

Although loss of sensation may be equally affected on the two sides of the body the vibratory sense may be unequally affected.

Loss of vibratory sense is never obtained over the sacrum except in disease of the spinal cord.

In his opinion the vibratory sense is not necessarily osseous in character, for it is preserved in complete bony fractures and is therefore probably a form of pressure sense transmitted through the skin and soft parts.

Williamson has confirmed these observations and feels that examination of the vibratory sense is of some value in the differentiation of spinal cord and peripheral nerve lesions, and hysterical anesthesia. He

finds the sensation often lost early, and before other forms of sensibility are affected, although it is always obtained in peripheral lesions of a single nerve when other sensory qualities are involved. From these observations he concludes that if in a local paralysis the vibration sense is lost, a peripheral nerve lesion is excluded, but if vibratory sense is present in the absence of other sensory qualities, a peripheral nerve lesion is probable.

*Trophic and Vasomotor Symptoms.*—Trophic and vasomotor disturbances occur more frequently in incomplete than in complete nerve lesions; but complete severance of a nerve is, nevertheless, accompanied by certain changes in the skin, nails, muscles, hairs, glands and even in the bones. Vasomotor disorders are not uncommon in total nerve lesion, and Tracy has devised the following novel method of testing the vasomotor reflex:

Stroking of the skin in a normal individual is followed by two sets of cutaneous reactions, said to be dependent upon the hormone content of the blood. First, vasodilatation of twelve seconds' duration; and second, vasoconstriction of two minutes' duration. The reaction time is recorded by a stop-watch and graphically represented. A dilatation of more than twelve seconds, or a constriction of more than two minutes is considered pathological, and it is thought that at least some of the tissue changes following complete nerve lesions are due to the vascular disturbances.

In the experimental section of a peripheral nerve studied by Rivers and Head, the analgesic area first becomes swollen from vasodilatation and edema, and the skin surface is rough and white from accumulation of epithelial scales. Later, the skin becomes wrinkled, inelastic and scaly, and the whole area—as the result of vascular stasis—of a deeper red than the normal skin. The hairs are also diseased and sweating is absent. In their work, a local sore finally developed, but probably from the use of a freezing mixture employed in making some of the sensory tests. Whether these skin lesions are due to the absence of a so-called trophic impulse or to the resulting vasomotor disturbance has not been definitely determined, but those who accept the presence of trophic fibres suggest that they may be located within the spinal ganglia because of the characteristic skin lesions so commonly observed in herpes zoster. Trophic changes are said to be more common in acute nerve lesions than in those which develop more slowly; and the skin lesions which proceed to ulceration are thought to depend upon the more frequent and unnoticed injury to which an analgesic area is subjected.

Duroux and Couvreur, from a series of experimental and clinical studies of the trophic changes following nerve injury, have observed in both instances the following lesions: ulceration, cyanosis, changes in the nails, and decalcification of bone with fracture. They divide trophic changes into pseudo- and true trophic disturbances. The former are recognized by the fact that they arise from local damage or infection of the skin in the denervated area. It was thought that these changes were due to nerve irritations rather than to destruction of the nerve, since trophic lesions failed to develop after complete section; and in the experimental and clinical cases there were evidences of nerve irritation. This opinion is supported by the fact that the trophic changes improved

or disappeared after section and resuture of the injured nerve. They do not accept the doctrine of true trophic nerves and feel that the symptoms are purely vasomotor phenomena.

**THE CLINICAL FEATURES OF INCOMPLETE NERVE LESIONS.**—Attention has already been called to the observation that the component fibres within a nerve trunk may suffer unequally in partial lesions of the nerve, and it is to be expected that the motor and sensory disturbances will vary according to the nature and degree of the injury. There are, however, certain more or less constant general symptoms—usually of an irritative character—which are common to most incomplete lesions of the peripheral nerves. Thus, pain, sweating, paresthesia, hyperalgesia, and, as Dejerine has shown, pain when pressure is made over the nerve below the lesion, and tenderness upon pinching the paralyzed muscles, are frequently observed. Souttar has added to these, dryness of the skin, accumulation of cutaneous debris, cyanosis of the affected area, and slender tapering fingers with glossy skin. Ulceration is said to be rare. White states that hyperalgesia without protopathic loss and increased excitability of the muscle to faradic stimulation are of common occurrence.

Stopford has made an interesting and instructive study of the irritative phenomena occurring after incomplete nerve division. He recognizes the difficulty of offering a satisfactory explanation for the occurrence of trophic, secretory, and vasomotor symptoms in such lesions, but feels that the theory of direct vascular implication is unsatisfactory. It has been shown experimentally that injury to a peripheral nerve is sometimes responsible for the development of endarteritis in the vessels of the affected area, and this has been thought to be due to implication of the nerve fibres supplying the arterial wall. It has also been observed that vasomotor and trophic changes are of more frequent occurrence as symptoms of nerve irritation than after complete nerve division; and that ulceration is more likely to develop in an area to which the nerve is just beginning to regenerate than in one in which the nerve impulse is completely abolished. Healing of the ulcer is said to occur with the complete return of protopathic sensation. The occurrence of gangrene in certain cases contributed also to the belief in the primary vascular nature of these so-called trophic changes. In Stopford's case, however, there was no direct injury to the blood-vessel, and lues was excluded; but thickening of the peripheral vessels within the affected area was intense and accompanied by marked trophic disorders. He concluded that the arterial change was directly consequent upon the nerve injury and that the irritative symptoms were dependent upon the secondary vascular disease. It is desirable, then, that incomplete nerve lesions be treated promptly, in order to remove the source of irritation and prevent the development of secondary vascular changes with their consequent trophic disorders.

**CAUSALGIA.**—The symptom of pain accompanying injury of the peripheral nerves has been the subject of investigation by a number of competent observers since Weir Mitchell first described a peculiar, per-



sisting, painful disease of the nerves which he designated as *causalgia*. Although most nerve injuries are, for a time, associated with pain, this symptom usually subsides. It is also well known that certain nerves exhibit this peculiarity more frequently than others; and this is particularly true of the median and the sciatic, and to some extent, of the ulnar, the crural, and rarely of the radial nerve. No satisfactory explanation has yet been offered for this peculiarity of individual nerves, and it is surprising that when two nerves suffer the same type of injury and undergo similar histological changes, one should be associated with excruciating pain while the other is entirely painless. Since the median and sciatic are the only two nerves which possess a distinct intraneural arterial trunk, it was thought that damage to the central vessel, with interference of the blood supply, might be responsible for the causalgic symptoms so commonly observed in these two nerves.

Stopford has given an excellent account of the disorder which he designates as *thermalgia*. The affection may be defined as a nervous disorder, usually the result of injury, characterized by intense pain, hyperesthesia, trophic and vasomotor disturbances, and occurring only in incomplete division of a nerve. It is said to be more common in war injuries than in the injuries of civil life. Since the median and sciatic (internal popliteal) nerves are most commonly affected, complaint is usually made of persistent, excruciating, throbbing or bursting pain in the arm or leg, which is generally aggravated by the dependent position of the extremity. The affected part is swollen; the surface temperature is elevated; and the extremity appears to be the seat of a deep suppurating process. Hyperhidrosis may be present. Rarely, bone and joint changes occur. The skin is sometimes glossy, exquisitely tender to pressure, and hyperemic. Mental states and changing atmospheric conditions are said to intensify the symptoms. Heat always increases the pain, but if the skin has not lost its sensibility, cool applications are said to be beneficial.

The affection has been designated by Souques as "*synesthésalgie*," because of a peculiar feature of the disease not unlike that common to painful affections of the trigeminal nerve, in that definite trigger or dolorigenetic zones are sometimes present. These "firing" zones may be in a part of the body quite remote from that which is the seat of pain. Souques observed a soldier who had received a wound of the left median nerve, but who wore a rubber glove upon the right hand because irritation from atmospheric changes or tactile impressions upon the right hand invariably induced a paroxysm of pain in the left arm. *Synesthésalgia*, it is stated, never occurs except as a symptom in *causalgia* or in incomplete nerve injuries. These remote firing zones show no gross abnormalities of cutaneous sensibility, and the attack, according to Cayla, is said to be more frequently induced by displacement of the skin in the contact zone than by tactile impressions. Humidity and dampness are thought to lower the firing point of the trigger zone. Tinel speaks of the trigger zone as a true "*champ causalgique*," but finds that it is present in only about one-half the cases, and that it may be situated upon

any part of the extremities or trunk. Occasionally there is a subjective feeling of soreness, or a sense of constriction in the contact zone, and objectively, a degree of superficial hypo-esthesia with deep hyperesthesia.

The pathology of the affection has not been definitely established and further studies in this direction are awaited. According to Stopford, partial division of the nerve and intraneural fibrosis are always observed, and the frequency of intraneural hemorrhage in war injuries probably explains the associated fibrosis. But identical pathological changes have been observed in many nerves which were not the seat of causalgia, and they also fail to account for the limitation of the affection to the median and internal popliteal nerves. Some condition other than nerve injury is therefore needed to explain the disorder. Stopford, has, in an earlier paper, attributed the vasomotor, thermalgic, and trophic changes occurring in nerve lesions, in general, to secondary arterial thickening consequent upon injury to the vasomotor fibres, and others have offered the same explanation for the development of these symptoms in injuries of the median and sciatic nerves. Stopford claims, however, that in injuries of these nerves the lesion is usually above the entrance of the neural vessels.

It had been generally believed that the arteries receive their sympathetic innervation near the proximal portion of the extremity, but Kramer and Todd have shown this to be incorrect and that the vessels receive this innervation at irregular intervals throughout their course from fairly constant nerve trunks. Leriche then suggested that causalgia may be due to injury of the peri-arterial sympathetic fibres, and this opinion has since been supported by the observations of Tinel, Cayla and others. The symptoms are thought to be of reflex origin, and transmitted through the vascular sympathetic fibres, or perhaps through the sympathetic fibres within the nerve trunk. Precipitation of the attacks by emotional states, and the thermic, vasomotor, and trophic changes accompanying the affection are advanced in support of this contention. Hyperexcitability of the sympathetic centers with extension of the discharge to neighboring centers, or even to homologous centers of the opposite side of the cord, are thought to account for some of the symptoms and to explain the synesthesalgic features of the attack. Price is of the opinion that in a few instances hematmata or hidden pockets of pus may be responsible for the condition.

*Treatment of Causalgia.*—Apparently, the only successful treatment of the affection has been derived from some form of surgical procedure, and Leriche was among the earliest to employ operative measures directed toward this end. At the January sixth meeting, 1919, of the Société de Neurologie, he suggested that relief may be secured by denudation and excision of the peri-arterial sympathetic plexus. Since then this operation has been performed with encouraging results by Le Fort, Cotte, Sencert, Levenant and others. Leriche has practiced denudation or sympathectomy in 30 cases, and resection of the vessel in 7 instances, with variable degrees of success. The operation is said to be of a physiological nature and, when successful, is followed by increased irritability of the

vessel wall, so that direct stimulation of the arterial sheath causes the vessel to contract to one-third or one-fourth its natural size. The segments above and below the operative field, however, retain their normal caliber. This convulsion of the artery is always sufficient to produce temporary abolition of the pulse, although sympathetic irritability varies in different individuals as well as in different arteries of the same individual, but appears to be greatest in the medium-sized vessels. The pulse is soon reestablished but feeble, and the affected part is colder than in the normal individual. From six to fifteen hours after the operation the characteristic physiological reaction appears and is characterized by a slight elevation of local temperature, a rise in blood-pressure, and increased amplitude of cardiac oscillations. These symptoms are thought to indicate the success of the operation and are only transitory, but are of greater duration after resection than after denudation.

**Sympathectomy** has also been practiced with success for the relief of profuse sweating, trophic disorders, causalgia, and muscle contracture when these disorders were the result of vasomotor disturbances. Certain ischemic paralyses and bed-sores have also been benefited by the operation. Tenani, who has extended the technic to include the nervous as well as the arterial plexus, claims, by this means, to secure more favorable results. Meige and Béhague have recorded an instance in which, following arterial denudation, the patient developed a peculiar vascular discoloration on the arm and chest. The skin lesion, which resembled a series of nevi, appeared to follow a vascular or sympathetic distribution rather than the course of a nerve.

Stopford recommends the treatment of causalgia by **local nerve operation** with the liberation of **perineural adhesions**, but feels that the interior of the nerve should not be explored, since further intraneural hemorrhage is to be avoided. The nerve should be protected from the formation of fresh adhesions, and if more than one-half its substance has been divided at the time of injury, resection and immediate suture are advised. In Stopford's opinion the intraneural scar is best treated by means of **normal saline ionization**. Preceding all operative treatment the patient should avoid mental excitement, and the affected part should be elevated and wrapped in moist lint. **Early operation** is advocated in every patient suffering from causalgia.

Tinel advises **section and immediate suture of the nerve near its termination** as the most effective treatment for this painful malady. He accepts the sympathetic origin of the affection, but is of the opinion that the pain is conveyed by means of collateral sympathetic fibres, and thus explains the failure to secure relief when the nerve is sectioned above the primary lesion. Although the greater part of the sympathetic fibres are located in the perivascular tissues, this is true only for the larger arteries of the extremities. The smaller peripheral vessels—such as the radial and ulnar—are relatively deficient in perivascular sympathetic fibres, and Tinel concludes that probably many of the peripheral sympathetic fibres are situated about the intraneural vessels, and for this reason advises resection of the nerve near its peripheral termination.

**Injection of the nerve with alcohol** was first adopted by Sicard, and practiced later by Pitres and Marchand, Grinda, Godlewski, Benoit, Morel and others. Sicard has had no success from section and immediate suture above the lesion, but claims to have secured excellent results from the injection of alcohol in 34 instances. He recommends its use in **selected cases only**, and especially when the pain is confined to the course of the nerve. The nerve is exposed and injected three or four centimeters above the lesion with a few centimeters of from 60 to 80 per cent. alcohol. Motor function is not necessarily destroyed by the injection, and even sometimes shows improvement. All but one of Sicard's patients were relieved, and, in some instances, for as long a period as three years. Pitres and Marchand have used the method successfully in 30 cases, and find that the alcohol does not delay motor regeneration; but that injection below the lesion is invariably unsuccessful. Ligation of the nerve above the lesion has been advised by Lorat-Jacobs, but this method has not been widely adopted.

**CLINICAL EVIDENCES OF NERVE REGENERATION.**—In the study of nerve injuries it is not only important that the physician be able to determine the nature of the lesion, but he should be trained to recognize the earliest evidences of returning function in the nerve and thus avoid unnecessary surgical intervention. In complete anatomic or physiological interruption of a nerve, restoration of function occurs, according to Sir Berkeley Moynihan, in the following order: Trophic and vasomotor innervation, deep sensibility, tactile discrimination and localization, voluntary motor power and, lastly, sensitiveness to cotton-wool. Motor function is said to always return before complete recovery of sensory impressions; and regeneration is generally more rapid in the young than in the aged. Price records an instance in which return of protopathic sensation occurred as early as one month after suture, and Purves Stewart has observed it as early as the third week.

Tinel's sign, "distant tingling on percussion," or "le signe four-millement," designated by the abbreviation D. T. P., is thought to furnish valuable early information as to the process of regeneration. MacDonald has made a careful study of Tinel's sign, and the method of making the examination is largely abstracted from his publication. Young nerve fibres are especially irritable to mechanical stimulation, and Tinel found that, if regeneration has begun, tingling is produced in the part to which the regenerating fibres are destined when the nerve is percussed at the site of the lesion. The reaction is usually obtained first at the site of the lesion, and may be elicited as early as the twentieth day after the injury, but it is generally not obtained until the fourth or sixth week. By the thirtieth day it may be elicited 2 centimeters below the lesion; at the sixtieth day, 5 centimeters below the lesion; and upon the ninetieth day, at a distance of 9.5 centimeters. There is thus a downward progression of the irritable area accompanying the newly growing axicylinders. The rate of progression varies, however, in different individuals, or it may be periodically accelerated or retarded in the same individual. It is stated that D. T. P. always occurs before there are

evidences of returning motor function or changes in the electrical reactions. The presence of the sign does not, according to Macdonald, indicate a reestablishment of anatomical continuity between the peripheral nerve terminal and the central stump, as many have thought; but indicates the reestablishment of continuity between the peripheral portion of the nerve and the cerebral centers. He also states that the downward progression of the irritable point occurs at the rate of 1 or 2 millimeters per day, and that after the new fibres have proceeded for a distance of about 10 centimeters—or, in other words, at the expiration of one hundred days—the sign can no longer be elicited at the site of the lesion. At the expiration of another hundred days the 10 centimeters which first recovered have also lost their irritability. This progressive loss of irritability continues in 10 centimeter segments until finally, when recovery is complete, D. T. P. can no longer be elicited. The sign is said to be of prognostic value also. Thus, an instance is recorded in which the sciatic nerve was injured near its origin. After twelve months the muscles of the leg were still atrophic and showed the reaction of degeneration, but it was found that percussion of the sciatic nerve within the popliteal space caused distant tingling; and a favorable prognosis for recovery without operation was given. It is said that if D. T. P. is obtained as early as the second month for a distance of 10 centimeters from the site of the lesion, complete recovery may be expected in a few months. Tinel's sign has been of some value in distinguishing the affected nerve in multiple wounds and in locating the exact level of the nerve lesion. Although D. T. P. is sometimes obtained in neuritis, it is in this condition, elicited throughout the extent of the affected nerve, and is accompanied by pain and tingling at the area percussed.

In making the test, Macdonald suggests that percussion should proceed from the periphery toward the lesion; for occasionally, when percussion is begun at the site of the lesion and tingling is once established, it may persist for a while and thus lead to error in judgment when the nerve is irritated more distally. During the test, the affected part, and especially in multiple lesions, should not be too vigorously shaken, for tingling may be produced in a nerve other than the one toward which the examination is directed. The clinical value of the sign has been discredited because of the confusion caused by wandering fibres during the regeneration period, and real difficulty is encountered in interpreting the sign when there are multiple lesions of individual nerves. In general, the presence of distant tingling is of greater value than the failure to elicit the sign. Price, however, feels that Tinel's sign is of doubtful diagnostic value.

As an evidence of regeneration, André-Thomas attaches considerable importance to sensitiveness of the skin when pinched; but the examination is of little value unless the reaction is obtained in a field which was previously anesthetic.

The reaction is thought to depend upon errors of localization, and is more commonly obtained at the periphery than in the center of the anesthetic field. It occurs in inverse ratio to the degree of sensibility present.

The muscles are also occasionally sensitive to pinching, and often to such a degree that a completely paralyzed muscle may thus be made to contract. In making the examination, it is to be remembered that the straying of regenerating nerve fibres may be responsible for the unexpected muscular contractions in a field remote from the one being tested. Thomas has also made interesting studies of the "errors of alignment" which occur in regenerating nerves, and his "topoparasthésies cicatricielles" have been referred to in an earlier paragraph. Straying fibres occasionally intermingle with those of an adjoining nerve in multiple nerve injuries, so that cutaneous nerves are distributed to the muscle, and vice versa, although there are no means of demonstrating motor nerve fibres in the true skin. This vicarious innervation is often responsible for the symptoms of parakinesis and synesthesia. Thus, a muscle under these conditions may not function so well in the performance of its usual associated activity as during the contraction of the muscle group to which it is in normal conditions unrelated. For example, in radial palsy the supinators may contract more vigorously during extension than during flexion of the forearm. Parakinesis is frequently observed, and is particularly common in sciatic and radial nerve injuries. Hyperexcitability of the muscles to cutaneous irritation is sometimes a symptom of nerve regeneration; and it is believed that the straying of sensory fibres and their irritation by the electric current explains the early return of electric excitability of those muscles in which return of voluntary power is greatly delayed. Thomas has further observed that even pricking or pinching the skin may, by stimulation of the sympathetic fibres, cause a contraction in a paralyzed muscle to which the nerve is regenerating.

**Treatment.**—GENERAL TREATMENT OF NERVE INJURIES.—*Presurgical Measures.*—Immediate operative treatment of nerve injuries, except in rare instances, is generally condemned, and it is therefore necessary to employ certain presurgical methods for protecting the injured part during the waiting period. Moynihan, Souttar, and Langley consider it essential to keep the paralyzed muscles perfectly relaxed to avoid injury from overstretching. Massage and moderate passive movements may be used to advantage; but Souttar finds little benefit from electrical stimulation. He recommends the whirl-pool bath, or "le'eau courant," which is said to accelerate the circulation, and to possess some of the properties of gentle massage. By its use the patient experiences an agreeable sensation; the muscles become soft and flabby; contractures are relaxed; and the improvement in the local condition is striking. In administering the bath, the affected part is surrounded by a stream of rapidly moving water at a temperature of 110°F. (43.3°C.). The duration of the bath is from twenty minutes to half an hour. Price advises excision of the primary surface scar with secondary closure of the wound as a means of reducing the formation of fibrous tissue.

**INDICATIONS AND CONTRA-INDICATIONS FOR SURGICAL INTERVENTION.**—Many of the injuries inflicted during the war were complicated by infection of the wound, and the general opinion prevails that no operation

should be performed upon the nerve until all danger of sepsis is removed, and until the primary surface wound has completely healed. Even after complete closure of the wound, and in view of the natural tendency of nerves to recover, different opinions were held concerning the desirability of surgical intervention. Dejerine expressed the view that it is better to postpone operation for at least three months after the injury; but Macdonald and Bramwell would delay operation as long as five or six months, or until sufficient time has elapsed for the appearance of regenerative symptoms. If, however, a positive diagnosis of a complete nerve lesion can be made, early operation is desirable. If the two ends of the nerve are separated or if there are evidences of neuromata, earlier operation is advised, but not until the primary wound has completely healed. Delorme then advises **excision of neuroma and suture of the divided nerve**. If the bone has been implicated in the injury the awaiting period should be prolonged for six or eight weeks. In the opinion of Sir Berkeley Moynihan, surgical intervention is indicated in three groups of conditions: (1) If there are evidences of complete nerve division; (2) in incomplete nerve division if, after a reasonable time, there are evidences of arrested progress; and (3) in causalgia. Elsberg claims that the earlier a divided nerve is sutured the better, and the more nearly complete will be the recovery; but infection often delays operation, and it is customary to postpone the operation for three months after complete healing of an infected wound. So long as there are evidences of regeneration the nerve should not be disturbed; and Macdonald recommends the restriction of all surgical procedure to those in which section and suture are indicated. Price advises primary suture at the first operation, regardless of the condition of the wound.

**CHOICE OF OPERATIVE METHOD.**—When operation is finally decided upon, good judgment is required in making a choice of the most appropriate method of treatment. The kind of suture, the bridging of lost tissue spaces, the removal of scar tissue, the prevention of end-bulbs, cross-suturing of nerves and preservation of the nerve pattern are matters of much concern. Chapple has suggested that in case of amputation, end-bulbs may be prevented by stripping back the nerve sheath, sectioning the nerve and closing the flap over the cut end. Huber finds that injection of the central stump with absolute alcohol likewise prevents the formation of amputation neuroma. With complete anatomical interruption and the formation of end-bulbs, resection and suture of the ends is generally recommended. Elsberg feels that freeing of adhesions, or perhaps partial resection, are quite effective in incomplete nerve lesions. Tinel, however, thoroughly disapproves of mere liberation of the nerve from scar tissue unless there are evidences of definite nerve constriction, and claims that the procedure is useless in the presence of neuromata or a cicatricial keloid. Resection and suture are, under these conditions, the more desirable methods. In Tinel's opinion, many cases in which nerve liberation is said to be successful are already in a process of regeneration at the time of the operation. Injection of cocaine into the central stump is said to prevent the occurrence of postoperative pains, which are

occasionally distressing. According to Noon, if a healthy tissue bed is secured it is not necessary to protect the nerve, but otherwise a fatty sheath should be employed. Price, from a statistical study of various operative measures, concludes that if after all reasonable tests have been made to determine the functional condition of a nerve there is still doubt as to its actual state, then resection is advisable and the prognosis depends somewhat upon the lapse of time between injury and operation.

The bridging of nerve gaps offers many interesting problems, and Huber has made some valuable experimental studies in this direction. The measures which have been adopted to remedy these defects are: the use of neuroplastic or nerve flap, grafting or nerve anastomosis, and multiple grafting. **Cross-suturing, suture at distance with catgut, tubular suture and tubulization, and nerve transplantation** are also recommended. Huber concludes that the first three should be condemned since they involve surgical injury to normal nerve tissue, and their value is not supported by laboratory experiments. Distant suture with catgut is generally unsuccessful. He recommends, however, tubulization and nerve transplantation as extremely desirable methods. Occasionally a considerable gap may be successfully bridged by **nerve stretching or changing the anatomical course of the nerve**. Sir Berkeley Moynihan condemns also the use of nerve grafting and anastomoses; and Price reports that all of his cases of anastomoses and nerve fusion were complete failures. Elsberg has had a measure of success from the use of **autonerve grafts**.

Huber has made a critical review of the various substances employed for tubulization of nerves and has experimented with the following methods: Decalcified bone, iodoform gauze and epidermis, magnesium tubes, hardened gelatin tubes, hardened artery of the calf, fascia lata with or without the fat layer, galalith—a casein preparation treated with formalin—, and Gargile membrane or the peritoneal membrane of the ox. His conclusion is that, of these substances, the **hardened artery of the calf and fascia lata** give most satisfactory results. Fresh arteries and veins are not so good because they frequently collapse. Sir Berkeley Moynihan's experience with the use of vein, fat, and Gargile membrane tubulization has been disappointing.

Transplantation and nerve grafting are advocated by Bramwell, and Huber finds that nerve transplantation is far superior to all other methods. The operation may be done with **auto-, homo-, or heterotransplants**, and of these, auto- and homotransplants give the most satisfactory results. Byrne records an instance in which a gap of 2.5 centimeters was successfully bridged by nerve stretching and feels that most cases can be successfully treated by this means. Huber, in a more recent article, records interesting studies upon the experimental transplantation of nerves conducted by himself, Lewis, Corbett, Stoakey, and Roberg. Their experiments warranted the statements that the use of auto-, homo-, and heterotransplants for the bridging of nerve gaps is a legitimate operation; that the autotransplant is the most useful; and that the heterotransplant is experimentally possible, but cannot be recommended for clinical use. It was also found that regeneration is possible if a degenerated auto-



transplant is made, but that this method possesses no advantage over the use of fresh tissue. The degenerated homotransplant is perhaps warranted in surgical practice, but the uncertain results obtained with the degenerated heterotransplant preclude its practical usefulness.

Instructive studies were made of the storing of nerve tissue for future use as transplant material; and it was found that tissue preserved for this purpose does not retain a latent viability. Liquid petroleum or 50 per cent. alcohol were used as preserving fluids, and auto- or homotransplants stored in either of these solutions were of sufficient value to warrant their consideration in surgical practice; but studies with the stored heterotransplant had not been extensive enough to permit an intelligent deduction.

The most suitable manner of protecting the transplant and suture lines from invading tissue was also investigated, and it was found that for this purpose the Cargile membrane hardened in 70 per cent. alcohol is most efficient, but unless hardened in this manner the membrane is absorbed so rapidly that its use as a barrier to connective tissue ingrowth is seriously questioned. Formalized arterial sheath may also be recommended; but autofascial and autofatty sheaths offer little or no protection, and tubular suture in which the formalized artery is used without a transplant is said to be of less value than the other methods. Huber and his associates concluded that ideal nerve repair is best secured by the end-to-end suture, provided the suture is relieved of all possible tension. Thus, in sciatic lesions of over 2½ inches, the defect may be overcome by fixing and immobilizing the knee; but in ulnar lesions just above the wrist-joint it is impossible to close any defects by flexion of the wrist.

In the stretching of nerves and nerve grafting it is desirable to know to what extent a nerve may be stretched without injury, and the success with which different kinds of nerves may be sutured. Langley has conducted some interesting experiments in an effort to answer these questions. He finds that rhythmic stretching of a non-paralyzed muscle is not necessarily harmful and that, before suture, fairly free extension and flexions of the joints may be permitted without injury to the nerve or muscle. After nerve suture, if there is no marked shortening, considerable movement may be allowed within a few weeks after the operation, for a moderate degree of movement is sometimes beneficial in lengthening the scar-tissue. In shortening nerves there is, however, great danger of rupturing the suture from even the slight movements.

The cross-union of different nerves has been investigated by Langley and Anderson, who have shown that afferent fibres do not unite with efferent fibres; that the crural nerve may establish functional anastomosis with the sciatic nerve and thus be used as a means of lengthening; but that the internal saphenous nerve, when joined to the sciatic, does not acquire motor function. Their experiments warranted the following conclusions: the central stump of efferent fibres will unite functionally with the peripheral end of any other efferent fibres of the same class; afferent fibres will unite with afferent fibres, but it is not known whether

fibres conveying one sensation will unite with fibres of a different sensory function; chemiotactic properties are greatest between fibres of the same functional importance; and a motor nerve united to a sensory nerve does not acquire motor properties.

**Direct neurotization by implantation of motor nerves** into paralyzed muscles has been attempted, and Elsberg and Gerster have contributed two recent papers upon this subject. The former experimented upon the rabbit and found that the results varied slightly, when he used the nerve which normally innervates the muscle or a neighboring nerve for transplantation directly into the paralyzed muscle. It appears to have been demonstrated, however, that direct neurotization of the muscle is possible even after a period of eight or ten weeks following the paralysis. Elsberg has further shown that a healthy muscle cannot be made to assume an additional nerve supply, for if a motor nerve is implanted into a normal muscle the implanted nerve cannot be made to transmit impulses until the nerve normally innervating the muscle has been sectioned and allowed to degenerate. Furthermore, if both the normal nerve and the implanted nerve are sectioned and immediately sutured, the normal nerve to the muscle resumes its function and prevents invasion of the implanted nerve. Gerster confirmed the experiments of Elsberg and demonstrated the presence of motor end-plates in connection with the implanted nerve.

**POSTOPERATIVE TREATMENT.**—The postoperative treatment of nerve injuries is not to be neglected and some of the more important measures have been suggested in the preceding paragraphs. Tension, both upon the nerve and muscles is to be avoided, **massage and passive movements should not be begun earlier than the third or fourth week**, and then very gradually increased. Electricity is said to be of some value, and Bordier and Gerard claim that regeneration is hastened by the use of **radiotherapy**. The affected part should be at perfect rest and wrapped in cotton wool. **Fresh air and a stimulating diet** are desirable, and later, more active passive movements, voluntary exercise, occupation, and encouragement in using the paralyzed limb will hasten the restoration of function.

**Prognosis.**—Two perplexing questions must necessarily occupy the attention of the physician who has the care of a patient suffering from a nerve injury: *First*, Is surgical intervention necessary, and, if so, what degree of functional return may be expected; and *second*, When is the best time to operate? Naturally, the answer to these questions depends upon his ability to diagnosticate the exact nature of the lesion, and the nature and extent of injury to which the nerve has been subjected. The age of the patient, his habits, and condition of general health must also be considered in formulating an intelligent opinion. Restoration of function is more likely to occur in the young than in the aged; but general ill health, constitutional disorders, and immoderate use of alcohol delay—if they do not entirely inhibit—the process of regeneration. Spontaneous recovery is said to be facilitated by electrical treatment, out-door life, massage, and superalimentation, although the study of war injuries has shown that the peripheral nerves possess a remarkable tendency to re-

cover, even in the absence of these measures. Evidences of recovery may, however, be delayed many weeks or even months after an injury, so that it is unwise to make an early or hasty prognosis, and a policy of "watchful waiting" has been generally adopted. The author recalls an instance of injury to the brachial plexus in which, after an interval of eighteen months, there were no evidences of regeneration. Complete return of function occurred, however, after an interval of two years, and Price records a similar observation.

A striking illustration of the extent to which a nerve may recover under apparently unfavorable conditions has been recorded by Ombredanne. The patient had had a fracture of the humerus with complete radial palsy. The humerus was sutured, the nerve liberated, and complete recovery occurred after one year. Because of a bony growth, an exploratory operation was later performed which afforded an opportunity to examine the radial nerve. It was found imbedded in a bony trough surrounded by dense scar tissue for a distance of two centimeters and presented at the upper level of the lesion a false neuroma.

The rate of recovery and recuperative ability are said to vary in different nerves, and Tinel finds that they are greatest in the radial and musculocutaneous nerves of the arm, and in the external popliteal nerves. In the median and ulnar recovery is often slow and incomplete, because of the frequency with which the internal architecture of these nerves is disarranged during the process of regeneration. Spear and Babcock have made similar observations, but Sicard finds slightly different recuperative ability in his series of cases, and concluded that return of motor function is more nearly complete in lesions of the sciatic and, to a greater degree, in the internal than in the external popliteal nerve. Recuperative ability is next greatest in the radial, then in the ulnar, and least in the median nerve, but in none of his cases was there perfect re-establishment of function. Elsberg concludes that there is never complete return of function in less than three months after suture. The average time, according to Gasset, for the first appearance of voluntary movement after lesions of the more important nerves is as follows: median, 6 months; radial, 8 months; external popliteal, 10 months; internal popliteal, 11 months; ulnar, 11 months; sciatic, 16 months.

Bramwell cautions against making a too hopeful prognosis merely because there are evidences of returning function in a nerve which has previously given every indication of complete division; for Price has found that when the nerve is exposed the pathological changes are always more extensive than the clinical symptoms had indicated. Although a nerve may be only partially divided it may suffer complete physiological interruption from concussion or edema; and thus, the symptoms dependent upon the edema sometimes show early improvement and encourage the hope of perfect recovery, while the actually divided portion often precludes the probability of complete restoration of function. Bramwell feels that recovery after secondary suture is always tedious and rarely is complete. From Tinel's study of 245 cases of nerve injury—some of which were observed more than a year—he is of the opinion that under

favorable conditions, almost all sutured nerves recovered satisfactorily. The failure to secure the desired results is explained by imperfect coaptation of the severed ends, imperfect vitilization, and persisting neuromata. All of his operative cases without end-to-end union were failures. He claims that early suture—during the first four months—offers a more favorable condition for rapid recovery, and that regeneration is always retarded when the divided ends are actually separated by the development of neuromata and scar tissue.

## DISEASES OF THE PERIPHERAL NERVES

### NEURITIS

**Definition.**—It appears that the pathological term “Neuritis” has been thoughtlessly used by the clinician as well as by the laity, to designate a variety of clinical disorders associated with nerve pain. Neuritis does not mean nerve pain; it means nerve inflammation; and inflammation of a nerve is usually accompanied by a group of symptoms in which pain is only one of the distinguishing features.

**Types of Neuritis.**—In a condition with so varied an etiology as neuritis, it is obvious that the clinical picture is determined, to a large extent, by the character and intensity of the inflammation, and the number, distribution, and function of the implicated nerves.

The symptoms of neuritis may appear suddenly, particularly when of toxic or infectious origin, or they may develop gradually over a period of several weeks, so that acute and chronic types have been recognized. The acute form is comparatively uncommon and generally subsides into the more familiar subacute or chronic affection. Either a sensory, a motor, or a mixed nerve may be affected; but all of the axons in a nerve trunk do not suffer to the same degree. Thus, even in those nerves which contain both sensory and motor fibres it is not infrequently observed that either one or both kinds of axons may be involved, although the motor fibres generally suffer more severely. For this reason it is convenient to speak of a sensory, a motor, and a mixed neuritis.

Occasionally, in traumatic or pressure neuritis, the disease is limited to a single nerve trunk, such as the ulnar, the radial, or the peroneal, and it is then referred to as a mononeuritis; but in the toxic and infectious forms the condition is more wide-spread and may involve several nerves in one or more plexuses. Thus, a mononeuritis multiplex is distinguished from a plexus neuritis in which all of the nerves of a single plexus are implicated. Multiple involvement of symmetrically placed nerves with the most pronounced symptoms in the distal portion of the extremities is known as multiple neuritis, polyneuritis, or peripheral neuritis, and this important type will be considered more fully in a subsequent section. The French neurologists, and particularly Sicard, have within recent years described an inflammatory condition confined to the nerve roots which is regarded as a true radiculitis. The symptoms are, in general, similar to those of neuritis, but are distinguished from the latter by the segmental distribution of the sensory and motor disturbances.

**Etiology.**—The causes of neuritis are numerous. Exposure and overwork are thought to be predisposing factors, but in all probability, are of importance only in so far as they lower individual resistance. Neuritis is rarely a primary disease, although an idiopathic form has been recognized. In the large majority of instances it is dependent upon one or more of the following etiological factors: Traumatism, toxic and infectious diseases, metabolic and cachectic states, and drugs and chemicals.

Various forms of external violence, such as fracture, dislocation, and prolonged pressure are sometimes the cause of neuritis, or a traumatic paralysis in which parenchymatous changes occur in the nerve trunk. Thus, brachial neuritis has developed from the continued use of an improperly adjusted crutch; and wrist-drop from prolonged pressure upon the radial nerve was, until recently, a familiar disorder. In the latter condition alcohol was often a predisposing factor, and it was not uncommon in dispensary practice to obtain a history of a preceding alcoholic bout during which the patient slept with the arm hanging over a park bench, the arm of a chair, or the edge of a bed. It was customary among this class of patients to hold the bacchanalian festival on Saturday evening, and the wrist-drop became known in certain clinics as the "Saturday-night arm." Dr. H. M. Thomas has related to the author an amusing incident in connection with wrist-drop occurring in a clergyman whose alcoholic indulgence otherwise would not have been questioned. Repeated inquiries failed to establish an etiological factor and Dr. Thomas, after explaining the frequent association of alcohol, prolonged pressure, and wrist-drop, urged the patient's free coöperation in the effort to account for the origin of his disorder. It was learned that the minister, then engaged to be married, had been visiting his fiancée who lived in a distant city. With his arm resting upon the back of a sofa and supporting the head of his fiancée, the combination of amorous intoxication and prolonged pressure proved too great for the resistance of an ordinary radial nerve. He departed with a fully developed wrist-drop. Temporary removal of the cause, and acceptance of Dr. Thomas's advice to use the other arm upon subsequent occasion resulted in complete restoration of function.

During general anesthesia the extremities are sometimes carelessly or unavoidably subjected to prolonged pressure with resulting injury to the more superficially placed nerves; and occasionally the lumbosacral nerves have suffered during parturition. Other causes of traumatic neuritis are found in certain occupations such as blacksmiths, cigar-makers, weavers, and oarsmen. Ulnar neuritis occurring suddenly after slight muscular exertion, or following a minor injury of the upper extremity is sometimes due to the presence of an unsuspected cervical rib. Rarely, the injection of sera has been responsible for the development of neuritis from direct injury to one of the superficial nerves. The author recalls such an instance in a soldier who had received an injection of antityphoid serum directly into the ulnar nerve.

Among the toxic and infectious diseases, influenza, erysipelas, typhoid fever, and diphtheria are frequent etiological factors. Neuritis has also

been recorded as a complication of pneumonia, malaria, and gonorrhea. Syphilis is not an infrequent cause, and may involve the nerve directly, or through the action of its circulating toxin. In leprosy, nodular enlargements are often found along the nerve trunks, and Climenko has called attention to certain syringomyelic features of leprosy neuritis. Multiple involvement of the peripheral nerves has been observed in tuberculosis in which the condition is generally parenchymatous in type and of toxic origin. It is said that genuine tubercles have not been found in the nerve trunks, although they are not infrequently surrounded by a plastic exudate. Toxic neuritis has also been reported as an occasional complication during pregnancy. Disturbances of metabolism and cachectic states are responsible for a large group of neuritides, and of the metabolic diseases, rheumatism, gout, and diabetes are of special importance. Grave anemias, the leukemias, and nutritional disorders are also occasional etiological factors.

Certain drugs and chemicals, particularly the heavy metals, appear to have a selective action upon the nervous system. Thus, the ethereal oils, analin, and carbon bisulphid have been known to cause parenchymatous changes in the peripheral nerves, and foreign sera also appear to exert a similar toxic action. Dyke has recorded a case of circumflex and suprascapular neuritis following the administration of antitetanic serum; and the author has seen bilateral facial paralysis from the same cause. Of the heavy metals, copper, lead, mercury, silver, and arsenic are the most frequent causes of neuritis.

**Symptomatology.**—**MODE OF ONSET.**—The clinical history of neuritis varies according to the type of the disease, its location and extent, and the nature of the etiological factor. In the acute type the onset of local symptoms is often preceded by a rise of temperature, increased pulse rate, headache, malaise, and other evidences of a mild infectious or constitutional disturbance. These general features subside as the local symptoms become more pronounced and, except in the milder cases, assume the features of the more protracted disease. Fever is not, according to the studies of Kent, a part of the clinical feature in neuritis. He finds that the body temperature is often subnormal, varying from 95° to 98° F. (35° to 36.6° C.); and that the intensity of the pain and the temperature excursions vary inversely. It is his opinion that with the fall in temperature the circulating blood is unable to hold in solution the accumulated products of katabolism which are then deposited within the tissues, and cause further irritation of the inflamed nerves. As the temperature approaches normal, these katabolic products are redissolved and the pain diminishes.

In the chronic affection the development of symptoms is more protracted and often preceded by a history of overwork, exposure, undue exertion, or evidences of a general bodily disturbance in which, however, the constitutional features of the acute attack are wanting. Ill-defined, transitory pain, at first so slight as to be ignored is an initial symptom, or there is sometimes a feeling of general soreness throughout the affected part with numbness and tingling in its distal portion. As the disease

progresses the pain becomes more persistent, of greater intensity, and more definitely localized along the course of the nerve, or disseminated throughout the extremity when several nerves are involved. Movement of the extremity is then particularly painful; the muscles are tender to pressure; the skin is usually hypersensitive; sleep is disturbed; and later there may be actual loss of cutaneous sensibility with motor weakness and changes in the tendon reflexes.

**SENSORY SYMPTOMS.**—The most prominent feature of nerve inflammation is pain, and the constancy of this symptom is largely responsible for the incorrect assumption that nerve pain alone suffices to establish a diagnosis of neuritis. When the disease is limited to the motor neurone, pain is, of course, absent, although it is not always present when the sensory fibres alone are involved. Thorn has recently described a case of syphilitic inflammation of the median nerve in which motor paralysis and anesthesia develop without the appearance of pain or paresthesia.

Ordinarily there is more or less discomfort throughout the course of the disease, although the pain varies in intensity and may alternate with brief periods of almost complete relief. It is described as of a dull, aching, boring, or throbbing character, deeply situated, and at times apparently in the bone or joint, or limited to a certain portion of the nerve which is then particularly tender to pressure. During a severe paroxysm, lightning-like flashes of pain are occasionally experienced throughout the course of the nerve. Nocturnal exacerbations are common; and movements which tend to pull, stretch or otherwise disturb the relation of the nerve are especially painful. Coughing, sneezing, and postural states leading to congestion of the affected part likewise add to the patient's discomfort. Tenderness of the muscles and deeper tissues is often a prominent symptom, and hypersensitiveness of the skin may be such that the weight of the bed clothes becomes unendurable, although actual pain is rarely projected to the cutaneous surfaces.

The diffuseness of the pain is often suggested by the manner in which the patient attempts to indicate its location. Thus, in mononeuritis the course of the inflamed nerve is only vaguely indicated by using the entire hand, or both hands rather than by the finger-tip method of the neuralgic patient. Sometimes, the palm of the hand is placed over a certain group of muscles or about a joint, and then moved in a rotary fashion over the painful area. Waterhouse and the author have previously directed attention to the particular technic adopted by those suffering from femoral neuritis. Both hands are placed about the ankle, whence they are moved upward to the knee, where several rotary movements are made over the medial and lateral surfaces of the joint, and, then one hand is directed along the anteriolateral aspect of the thigh to the ligamentum inguinale.

The inflamed nerve may be diffusely swollen, and occasionally disseminated, fusiform, or nodular enlargements are found along the trunks of palpable nerves, particularly in syphilitic and in leprous neuritis. Considerable experience in the palpation of nerves is, however, necessary in order to detect these abnormalities; and caution is to be observed in

weighing the value of nerve tenderness as a diagnostic feature of neuritis. The normal nerve is painful upon too vigorous pressure, and the hypersensitive nerves of the neurotic are of common occurrence. Increased irritability of the peripheral nerves has also been described in poliomyelitis.

Objectively, the skin is either glossy, dry and scaly, or moist and clammy; and local sweating is sometimes profuse. Trophic and vasomotor changes are not uncommon. Redness and swelling of the affected part and, in rare instances, effusion into the joints have been described. Herpes and skin eruptions are unusual. There may be diminution or, in severe cases, loss of all forms of cutaneous sensibility in restricted areas; and dissociation of sensation is said to occur. Changes in the vibratory sense and the ataxic form of the disease are significant features in the symptomatology of multiple neuritis.

**MOTOR SYMPTOMS.**—Weakness or inability to move the affected part is sometimes an early complaint, although the motor disability is at first more apparent than real and due largely to the painfulness of the movement rather than to actual paralysis. In severe cases there is complete paralysis in which, however, all of the muscles innervated by the diseased nerve do not necessarily suffer to the same degree. The onset of the paralysis is often progressive, and usually the muscles at the distal portion of the extremity are first and most severely affected. The muscle is soft, flabby, atonic, and in the beginning, may show hyperexcitability to electrical stimulation, but later exhibits the characteristic reaction of degeneration. If the atrophy is pronounced there may be complete absence of electrical response when the muscle is first tested; but this does not necessarily indicate that the muscle has suffered irreparable damage, since repeated stimulation may elicit a feeble contraction; and not infrequently voluntary movement precedes the return of electrical excitability.

The tendon reflexes are usually diminished or lost, but are said to be slightly increased in the earlier irritative stages of the disease. In protracted cases active or passive contractures often complicate the clinical picture, or when a single nerve, such as the radial or peroneal, is affected the part may assume, from the beginning, the characteristic posture of the familiar wrist- or foot-drop. Irritative muscle contractions, probably of reflex origin, have also been described; and fibrillation, though rare, is said to occur. The peculiar motor phenomena, described by Babinaki and Froment, characterized by hypertonia or contracture, paralysis of voluntary motion, increased reflexes, and pain are thought to be of neurotic or physiopathic origin. Molhant is of the opinion that they are of a reflex nature and dependent upon irritation of the sensory nerve terminals in the skin, subcutaneous tissue, and muscle. A destructive lesion of this system of fibres alone is said to produce tabetic dissociation of sensation, hypotonic paralysis, diminished reflexes, and vasomotor disturbances.

**Diagnosis.**—Ordinarily, the diagnosis offers few difficulties. The history of the onset, the progress of symptoms and their limitation to the



distribution of one or more of the peripheral nerves, tenderness of the nerve trunk upon palpation, the character of the pain, and the changes in cutaneous sensibility are significant features. If, in addition to these, there is hypotonia with motor paralysis and the reaction of degeneration to electrical stimulation a diagnosis of neuritis may be made with reasonable assurance.

In the early stages when pain is a prominent symptom and unaccompanied by motor disturbances, neuritis has been mistaken for a rheumatic or bone affection; and unfortunately, the pains of the tabetic are not infrequently regarded as a "slight attack of neuritis." The pain, sensory changes, and muscle paralysis of syringomyelia require careful differentiation; and the neuralgic attacks in chronic neuritis in which the motor symptoms are wanting, sometimes obscure the clinical picture. A systematic and orderly examination will, however, do much to simplify the diagnostic problem. The presence of nerve tenderness, the location, character, and duration of the pain, the Argyll Robertson pupil, the serologic reactions, the type of sensory disturbance, and the spinal or neural grouping of the paretic muscles are important differentiating features.

**Treatment.—GENERAL MEASURES.**—The choice of suitable therapeutic measures rests largely upon the diagnostic skill of the physician and the success of his efforts to determine the etiological factor. When the underlying condition is established its eradication is, of course, of first importance, but the cause of the inflammation often remains obscure although its infectious, toxic, or metabolic origin may be suspected. It is desirable, therefore, that certain general measures be adopted regardless of the location or duration of the disease, though a more selective therapy is to be practiced in the treatment of the local condition. In both the acute and chronic stages, **rest, diet, sleep, and elimination** are to be regulated. In even the milder cases, recovery is facilitated if the patient can be persuaded to remain in bed. The value of rest is often underestimated, particularly in the subacute and chronic types. Not infrequently a protracted neuritis, which continues rebellious to all forms of medication, so long as the patient is permitted to engage in his daily activities, yields promptly when these measures are supplemented by complete rest in bed.

In the beginning, a soft diet is preferable, and throughout the rest period it should be moderate, non-irritating, and easily digested. Kent recommends a diet of high caloric value as a means of encouraging physiological generation of heat to counteract the subnormal temperature said to be present in neuritis. For this purpose, he orders a superabundance of fats in the form of olive oil, butter and bacon, and claims that by this means he has procured an elevation of temperature with consequent alleviation of symptoms. Additional evidence in support of this doctrine was derived from his study of nerve lesions during the World War, where he found a preponderance of neuritis and neuralgia among those troops whose diet was deficient in fats, or of low caloric

value. Sleep is essential, and the proper amount should be procured, if necessary, by the administration of hypnotics for a brief period, supplemented by the use of analgesics when pain is a disturbing feature. A mild cathartic or a saline laxative may be given daily, and the free use of internal hydrotherapy is to be practiced.

**LOCAL TREATMENT OF THE ACUTE ATTACK.**—The pain and disability accompanying the acute attack, and particularly in neuritis of the lower extremities, usually serve to make the patient accept willingly the instruction to remain in bed; but general bodily rest alone is not sufficient. The affected part should be rendered as immobile as conditions will permit, and in such a position as to relieve tension and prevent the subsequent development of contracture. It has been shown, experimentally, that injured nerves regenerate more rapidly under the influence of heat slightly above the body temperature. Heat is also of value in diminishing the intensity of the pain. Thus, it is often helpful to keep the part wrapped in cotton wool, or warm moist poultices, and in milder cases, the Paquelin cautery may be cautiously applied. Counterirritation is, however, not ordinarily practiced in the actively acute stages. Leeches, scarification, and blistering were recommended by the earlier writers, and local sweating was thought to be of value in some instances. Massage and all measures likely to lead to congestion of the affected part are contraindicated. Electricity is often distinctly harmful in the acute stages; although, as the pain subsides, the faradic brush may be used to advantage if paresthesia is a prominent feature. When anesthesia is pronounced, care must be taken to protect the part from injury and from the higher temperatures of local applications. The skin surfaces should be kept clean, and bathed daily with alcohol to prevent the development of trophic disorders.

**LOCAL TREATMENT OF THE CHRONIC AFFECTION.**—It is desirable to begin the course of treatment with a brief period of rest in bed during which time movement of the affected part should, at first, be reduced to a minimum. Massage and passive movements may, however, be prescribed during the rest period. If there is motor weakness or paralysis, mechanical means should be adopted to maintain the normal position of the part and prevent the overaction of unopposed muscles. Electrical stimulation of the parietic muscles was, until recently, generally recommended, but clinical studies of nerve injuries during the World War seem to indicate that it is of questionable value. If electricity is prescribed the faradic current should not be used for muscle stimulation since it is often painful, and a muscle which responds to this form of current is, ordinarily, not in need of electrification. Brief stimulation with the galvanic current is more suitable and may be practiced daily until there are evidences of returning voluntary movement.

**MEASURES ADOPTED FOR THE RELIEF OF PAIN.**—In subacute and chronic neuritis various active counterirritants have been employed. The continuous electric current along the course of the inflamed nerve is often beneficial. Martin advocates the use of the static wave, the high frequency current, and the electric-light bath. Local applications of fum-

ing hydrochloric acid have been made over the skin of the affected area, and Sainsbury claims some success with this method. The applications are made two or three times weekly. Kent, however, finds it of little benefit. Jensen recommends the injection of camphorated oil beneath the skin of the painful region, and has used it successfully in sciatic neuritis. Subcutaneous injections of Schleich's solution, cocaine, and novocain have also been practiced with variable results. Intraneural injection of urea-hydrochlorid has been resorted to in a few instances, but it is the author's opinion that it is more often harmful than beneficial and should not be practiced upon mixed nerves, since the motor fibres may be seriously damaged. He has seen paralysis of eight months' duration follow injection of this drug into a painful radial nerve.

These measures are often supplemented by some form of internal medication, particularly in the acute stages when pain prevents the required amount of rest and sleep. The antipyretics, analgesics, and coal-tar products offer a long list from which a selection may be made. Antipyrin, phenacetin, acetanilid, and pyramidon each has its advocates, and is prescribed alone or in combination with codein. Kent, however, does not approve of the use of antipyretics since, according to his theory, they lower the body temperature and thus often fail to relieve the pain. Morphine should be used only in case of necessity. During convalescence a general tonic course is advisable.

**Prognosis.**—The duration of the disease is variable, and depends upon the etiologic factor, the extent of the inflammation, and the damage which the nerve has suffered. Ordinarily, the prognosis for recovery is good. In the milder degrees of pressure neuritis the symptoms may be of only a few days' duration, while those of toxic, infectious, or metabolic origin usually run a more protracted course of from six to twelve weeks or even several months. Estimation of the probable duration of the illness is often difficult, and occasionally, complete restoration of function does not occur; so that it is necessary to make guarded statements when predicting an early recovery. On the other hand, what at first appears to be a hopeless condition may, after many months, exhibit a surprising degree of functional return. The author has among his records the history of a patient who suffered from brachial neuritis following injury of the shoulder joint. The arm was completely paralyzed, and after a period of eighteen months showed no evidence of recovery. Eight months later, or twenty-six months after the injury, word was received from the family physician that the patient had regained almost complete use of the paralyzed arm.

**Pathology.**—Because of the generally favorable prognosis in neuritis, few opportunities arise for direct examination of the diseased nerve. Sufficient material has, however, been studied to permit a division of the pathological changes into three main types of inflammatory reaction. Thus, it is customary to speak of a *perineuritis* when the inflammation is most pronounced in the extraneural sheath, of an *interstitial neuritis* when the intraneural septa are principally affected, and finally, of a *parenchymatous or degenerative neuritis* when the axis-cylinder and mye-

lin are primarily involved. The adventitial lesion, whether of the perineuritic or interstitial type, is characterized by a genuine inflammatory reaction, and is most frequently observed in the mononeuritides. Occasionally, the nerve fibres are replaced by fatty tissues, and it is then designated as lipomatous or Lyden's neuritis. In the parenchymatous form, especially frequent in the toxic and polyneuritides, the histological changes are, according to Buzzard, indistinguishable from those of a true wallerian degeneration. He also describes a second type of reaction in which the axis-cylinders are swollen, stained more intensely, and in some instances vacuolated; or the neurilemma may be distended by fine globular masses which give the staining reactions of fat. This fatty disintegration is probably similar to that occurring in other tissues subjected to the influence of circulating toxins, and has been observed in the neurilemma cells before fragmentation of the myelin has begun. The cytological reaction is usually of moderate intensity, and active cell infiltration with suppuration is said to be rarely observed. Thus, in the adventitial type the nerve fibres are not often directly damaged by the acute inflammation, although they may suffer to a considerable extent from the contraction of scar tissue and moderate vascular thickening during the process of repair.

As a result of these microscopic changes there is not infrequently an alteration in the external appearance of the inflamed nerve; so that upon gross examination it is often swollen, edematous, congested, or in rare instances, hemorrhagic. The inflammation is sometimes limited to a portion of the nerve, or there may be several isolated areas of inflammation. Occasionally, the entire nerve trunk is affected. Thus, a focal, a disseminated, and a diffuse neuritis have been described.

Local infections, and particularly septic wounds of the extremity are at times associated with a type of neuritis which is thought to depend upon propagation of the infection along the sheath of the nerve. This ascending form, or *neuritis migrans* has not, however, been generally accepted, and it is noteworthy that the neurological literature of the recent War has not altogether sustained the position of those who advocate the occurrence of this type of neuritis. A descending neuritis, in which the infection is propagated along the course of the nerve as far as the interstitial muscular tissue, has also been described. It is then known as *neuritis fascians*, or Eichhorst's neuritis, and finally, a sympathetic neuritis is said to occur in which the infection is transmitted from the inflamed nerves upon one side of the body, through the nerve rootlets and the spinal cord, to nerves of the opposite side.

### NEURALGIA

In both neuritis and neuralgia pain is the dominant symptom. The terms are, therefore, often used indiscriminately and without due regard for the clinical and pathological features of the two conditions. *Neuralgia* is a clinical term meaning an acute paroxysmal pain in the course of one or more of the peripheral nerves.

The paroxysmal nature and short duration of the neuralgic pain, its shooting, stabbing, darting character, and the free interval between attacks serve to distinguish it from neuritis, although in the latter condition the pain is sometimes of the neuralgic type. In neuralgia, there is no objective loss or diminution of cutaneous sensibility; the nerve trunk is not tender to pressure; the tendon reflexes are unaltered; and there is no muscle weakness or paralysis. Occasionally, the skin over the affected area is hypersensitive to light touch, and during a severe paroxysm spasmodic contraction of the muscles has been observed. Any peripheral sensory nerve may be the seat of a neuralgic attack, and several varieties have been described. Thus, crural, sciatic, abdominal, intercostal, brachial and cervico-occipital types are recognized. These are more fully described as diseases of the individual nerves, while a separate chapter has been assigned to the classical neuralgia of the trigeminal area (Chap. X, Vol. X).

The *pathology* and *etiology* of neuralgia are not fully understood since, with the exception of the trigeminal affection, a microscopic study of the nerve is rarely obtained. Of the nerves which have been examined, many have shown no histological changes; and these observations have contributed to the belief that neuralgia is purely a symptomatic disorder, probably of functional origin. This view is contradicted, however, by isolated instances in which minor structural changes and moderate thickening of the intraneural vessels have been described. It is believed, therefore, that the affection is in all probability dependent upon a mild inflammatory reaction in which circulatory changes play a prominent part; and that at times it may even be quite impossible to make a clinical distinction between neuritis and neuralgia.

With the exception of trauma, the *causes* of neuralgia are, in general, similar to those of neuritis. Toxic, infectious, metabolic, and anemic states are of etiologic importance, and climatic and barometric changes have a decided influence upon those in whom there is predisposition to the disease.

The *treatment* of the affection is largely constitutional and directed toward the removal of any source of irritation or infection, and the correction of any obvious defective state. The teeth, tonsils, and cranial sinuses require, therefore, careful investigation in the search for hidden sources of infection. Since many neuralgic patients are of the functionally neurotic type, a full rest cure, with the additional measures usually employed in the treatment of the neuroses, may be adopted advantageously. This is to be followed by a general tonic course, change of climate, and stimulating exercises. The galvanic current, massage, and local counterirritant applications have been recommended, but are of doubtful benefit.

#### TUMOR OF NERVES

The word *neuroma* was first used in 1803 by Louis Odier in a strictly clinical sense to designate any enlargement anatomically connected with a nerve trunk. It included, therefore, both the benign and malignant tumors found along the course of the peripheral nerves, and in no way indicated their histological structure or probable neurogenous origin. The

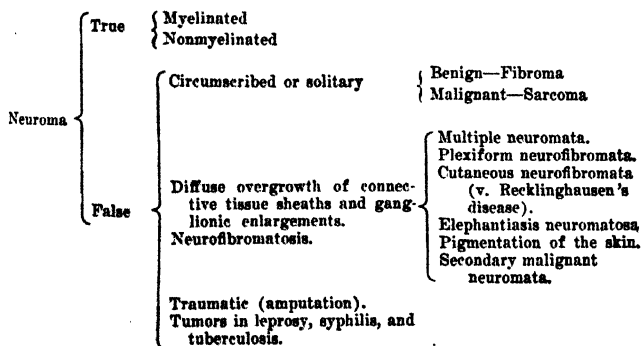
beginning of a more scientific classification was made in 1849 by R. W. Smith when he expressed the opinion that most nerve tumors were of the connective tissue type, and of spontaneous origin, or the result of injury to the nerve trunk. He continued, nevertheless, to use the term *neuroma* in its more general sense, and contended that tumors composed of true nerve tissue did not occur. It was not, therefore, until the appearance of Virchow's studies in cellular pathology that any real effort was made to classify these morbid growths upon a purely structural basis. Virchow divided them into two main types as follows:

- (1) The true neuromata, composed of new nerve tissue containing nerve cells, and medullated or nonmedullated nerve fibres.
- (2) The false neuromata which includes all other tumors and particularly those of connective tissue origin.

He was mistaken, however, in the opinion that the true neuromata constituted the predominating type.

Nerve tumors may be single or multiple, and as many as three thousand neurofibromata are said to have been counted in a single instance. The classification of these new growths has been further complicated by the discovery of nerve fibres in the cutaneous and subcutaneous fibromata, in certain forms of elephantiasis, and by the inclusion of plexiform neuromata, amputation neuromata, and sarcomata.

A monograph by A. Thomson "On Neuroma and Neurofibromatosis" gives an instructive résumé of the subject up to 1900, and the following classification of nerve tumors is an abridged form of that adopted by Thomson:



True neuromata are extremely rare and are said to occur only in connection with the sympathetic nervous system. They are accordingly composed principally of nonmedullated nerve fibres; but myelinated fibres are occasionally observed, and ganglion cells have been found in rare instances. The tumors may be single or multiple, and vary in size from one to ten or twenty centimeters in their largest dimensions. They occur most frequently during childhood, and are usually situated within the abdominal cavity about the larger sympathetic trunks, but are some-

times subcutaneous. The tumor may be soft or firm; it is usually not sensitive, and is generally unaccompanied by pain or other evidences of its connection with the nervous system. Because of the absence of symptoms and the benign nature of the growth many of the smaller tumors are discovered only during routine postmortem examinations.

False neuromata form by far the larger and more interesting class of nerve tumors, and the more common forms arising directly from the nerve trunk are the fibromata, neurofibromata, and angiomas. Both benign and malignant types occur; and the benign tumors occasionally exhibit retrograde cellular changes resulting in the formation of myxomatous, lipomatous, or cystic areas, which may show evidences of true malignancy. Ordinarily, the innocent forms are of slow growth and sometimes exist for several years without giving rise to symptoms of a distressing nature. They are more common along the course of the nerve than at its periphery, and are attached to the surface of the nerve trunk or imbedded in its substance. The intraneural fibromata sometimes merely separate the nerve fibres without doing great damage to the axons or causing serious disturbances of function; but, ordinarily, they are accompanied by the symptoms of moderate nerve compression. Pain, paresthesia, and variable degrees of motor disability are the usual features, but complete sensory and motor paralysis is rare. The peripheral nerve terminals are occasionally the seat of multiple painful fibromata, and Wood has collected 35 cases of these painful subcutaneous nodules.

The cause of false benign neuromata is not known, but trauma is said to be a predisposing factor. They may have their origin in the perineurium, epineurium, or endoneurium, and are composed chiefly of connective tissue. Thus, it is customary to refer to the entire group of single or multiple neuromata occurring in the subcutaneous tissues, or along the course of the nerve trunk as fibromata, neurofibromata, fibroma molluscum, or fibromatosis nervorum. The true nature of the cutaneous fibromata, or molluscum fibrosum, was first demonstrated by v. Recklinghausen in 1882 who designated them as neurofibromata of neurogenous origin. He later concluded, however, that they arose from the endoneurium and connective tissues sheath only, and should, therefore, be regarded as true fibromata. Weller, however, calls attention to the fact that Verocay has since demonstrated that they contain new nerve tissue, and prefers the term *neurinoma* suggested by Adami. The treatment of tumors of nerves is essentially surgical.

### HERPES ZOSTER

**Definition.**—Zona, shingles, acute posterior poliomyelitis, herpes zoster, or the radiculoganglionic syndrome is an acute inflammatory disease of the posterior root ganglion, probably of infectious origin, characterized by pain, and a distinctive eruption in the peripheral distribution of the affected nerve.

**Etiology.**—Herpes may be primary, or secondary and symptomatic of a constitutional, infectious, or local disorder. A toxic form has also

been described. Much uncertainty still exists as to the etiological factor in the primary form although its infectious nature is generally recognized. Head and Campbell have demonstrated an organism in the posterior spinal ganglion and nerve roots, but its specific nature has not been established. The studies of Rosenow are interesting but unconfirmed. He claims to have reproduced herpes in lower animals by the injection of pus from carious teeth, diseased tonsils, and other foci of infection in patients suffering from the disease. Animal inoculation with the spinal fluid obtained from a patient during the acute stages of the eruption is said to have produced the characteristic skin lesion and pathological changes in the posterior spinal ganglia. Lain is of the opinion that herpes, rheumatism, and erythema nodosum are due to the same cause, and probably dependent upon dental or tonsillar infections.

In 1909, Bokay directed attention to the occurrence of herpes and chicken-pox in the same individual, and suggested a common etiology for the two diseases. Le Feuvre, in addition to his seven cases, collected 43 such instances from the literature; and since then the observation of Goldberg, Wilson, Cooke, and Taylor have furnished additional clinical evidence of the association of the two conditions.

That herpes may develop during the course of a general or local disorder is well known; and this symptomatic type has been observed in a number of conditions. The eruption appears occasionally in tabes, in general paresis, and in other forms of cerebrospinal syphilis; and syphilis as a cause of herpes has been studied recently by Boner who states that the spirochete has been demonstrated in the posterior spinal ganglia. This does not establish, however, the syphilitic nature of the herpetic eruption, since the organism has also been demonstrated in the ganglia of tabetics in whom herpes has not developed. Immerman also attributed the herpetic eruption, in a case of tabes and in three cases of general paresis, to direct syphilitic affection of the ganglia. From a study of the spinal fluid in 42 cases of herpes in syphilitic and nonsyphilitic patients, Brown and Dujardin conclude that syphilis is not a direct cause of the eruption; that it may be a predisposing factor by rendering the ganglia more accessible to the specific herpetic virus; and that in all cases of herpes the possibility of an earlier syphilitic infection must be considered. It was also noted that the lymphocytes in the spinal fluid vary from 1 to 470 per cu. mm.; that the greatest increase occurs in the cases of aborted herpes; and that the development of herpes during a course of arsenphenamin therapy is unusual.

Meningitis, caries of the vertebra, spinal cord tumor, and fracture or dislocation of the vertebra are sometimes the cause of a secondary herpetic eruption. Boursier and Ducastring have described an instance in which it was thought to be due to concussion of the spine, and Boas records its appearance following an epidural injection of normal salt solution. A so-called reflex herpes from disease of the viscera, and herpes of neuritic origin have been described, but in all probability are dependent upon one of the better known etiological factors. Herpes sometimes develops during a course of arsenical therapy, during preg-



nancy, and according to Gloaguen after the administration of anti-typhoid serum.

**Symptomatology.**—The infectious nature of the disease is suggested by the constitutional features of the onset in which, fever, malaise, occasional lymphadenitis and gastro-intestinal disturbances are the more common symptoms. Within three or four days the eruption, generally unilateral and confined to a dorsal root zone, makes its appearance. Pain, of a burning, stabbing character, may be an initial symptom, and, with the constitutional disturbance, subsides upon the appearance of the eruption; but it may continue throughout the disease, and occasionally persist as a distressing postherpetic feature. Ordinarily, there is no loss of tactile sensibility in the eruptive area; but the recognition of pain and temperature may be temporarily diminished or lost, and occasionally, there is marked hyperesthesia to tactile impressions.

The eruption makes its appearance gradually as a series of vesicles upon an erythematous base, and is usually fully developed within five or six days. The vesicles are generally discrete, or in clusters, and contain a clear fluid which, however, is often purulent from secondary infection, or in rare instances hemorrhagic. In severe cases the eruption is sometimes confluent or even gangrenous. A week or ten days after the appearance of the vesicles the skin lesions begin to fade, and in the milder forms leave no permanent skin marking, although moderately depressed or scarred areas may persist for a variable period. In the gangrenous type there is permanent and sometimes marked disfigurement with persistent cutaneous anesthesia resulting from destructive changes in the skin and subcutaneous tissues.

Thus, the progressive development of the eruption and its usual limitation to a restricted zone about the thoracic wall have been responsible for its designation as herpes zoster. Multiple involvement of ganglia have, however, been observed, and the eruption may appear upon any part of the cutaneous or mucous surfaces. It is most commonly situated upon the trunk, arms, neck and head; but the lower extremities, and especially the genitalia are not infrequently affected. Herpes of the face, particularly in the distribution of the ophthalmic nerve, herpes corneæ, and auricular herpes are of special interest. In ophthalmic herpes the eruption is sometimes intense, often confluent, and the gangrenous type with persistent postherpetic pain is not uncommon. Herpes of the neck, occiput, or auricle is sometimes associated with facial paralysis or evidences of involvement of the cochlear and vestibular nerves. J. Ramsay Hunt has made a special study of this type of the affection, and is of the opinion that the combination of auricular herpes and facial paralysis rests upon an herpetic inflammation of the geniculate ganglion. The author has, however, never succeeded in demonstrating the slightest diminution of cutaneous sensibility upon the face, auricle, auditory meatus, or tympanum in these cases, nor has he observed any sensory disturbances in the zone assigned to the geniculate ganglion when the facial paralysis is not associated with herpes. Ocular palsies, evidences of meningeal irritation, and muscular atrophy have been described

among the complications of herpes; and it is thought that these symptoms may be due to involvement of the meninges, spinal cord, or nerve trunk.

**Treatment.**—The self-limited nature of the affection and its obscure etiology have thus far precluded the adoption of a specific form of therapy. Treatment of the idiopathic type is, therefore, entirely symptomatic. Both general and local measures are employed. Since herpes is often of toxic origin or symptomatic of a primary local disorder, a thorough clinical and laboratory study should be made. Rest in bed is desirable. A brisk purgative and active elimination are prescribed at the outset, and the administration of urotropin has been recommended because of its antiseptic properties and subsequent elimination in the cerebrospinal fluid.

The pain of the acute stages may require the use of acetanilid, phenacetin, pyramidon, codein, or even morphin in severe cases; but these drugs are of questionable value, and morphin is distinctly contraindicated in postherpetic neuralgia. Repeated attempts to relieve postherpetic pains by the superficial injection of alcohol into the affected nerve, or by injection of the dorsal root ganglion have met with rather discouraging results. The author has injected the supraorbital nerves of 3 patients suffering from residual neuralgia following gangrenous herpes; but the results were not altogether satisfactory. In none of the cases was the pain entirely relieved, but all three experienced a degree of comfort which they had not hitherto known. One of the patients, who was cyanotic from prolonged and excessive use of coal-tar products, was enabled to discontinue all medication. The Paquelin cautery and electricity, along the course of the nerve or over the dorsal root zone, are said to be of occasional benefit.

Resection of the nerve or posterior spinal root has been practiced with equally variable results; and in herpetic neuralgia of the trigeminal nerve avulsion of the sensory root of the gasserian ganglion may have to be resorted to.

Local applications of a nonirritating nature are often grateful. The eruptive area may be dusted with a mixture of talcum powder and boric acid to which 2 per cent. of camphor is added if itching is severe, or a 3 per cent. ointment of lanolin and thymol is equally soothing. A 1 per cent. ointment of novocain or eucain has been recommended if there is much local pain.

**Prognosis.**—The prognosis in herpes is usually good. In the majority of instances the disease runs an uncomplicated course in from one to three weeks and one attack of the idiopathic affection is said to confer immunity.

**Pathology.**—The earlier pathological study of herpes was concerned largely with an examination of the local skin affection, and although its neurogenous nature had been surmised, it was not until 1863 that v. Baronsprung first demonstrated the lesion in the posterior root ganglion. This was followed by the classical studies of Head and Campbell in 1900 which not only established the pathology of the disease in the posterior spinal ganglia, but furnished a means for the more accurate determina-

tion of the segmental innervation of certain cutaneous areas. The pathology of labial and nasal herpes occurring in the infectious disease, and particularly in pneumonia, has been studied by William T. Howard who found local inflammatory changes in the gasserian ganglion.

The lesions in idopathic herpes is characterized by cellular infiltration of the ganglion and its sheath with a variable amount of destruction of cells and fibres and the subsequent formation of scar tissue. In the milder cases the ganglion may recover with little or no evidence of the previous injury. The inflammation is often hemorrhagic, and if intense, may be accompanied by lymphocytosis in the spinal fluid, Kernig's sign, or other evidences of meningeal involvement. The anterior root is, however, rarely the seat of active inflammation, but occasionally suffers from edema and pressure from the swollen ganglion.

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## CHAPTER II

### DISEASES OF THE SPINAL CORD

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Progressive muscular atrophy, p. 289—Myelitis, p. 293—Acute myelitis, p. 293—Compression myelitis, p. 299—Chronic myelitis, p. 303—Amyotrophic lateral sclerosis, p. 304—Spinal meningitis, p. 310—External pachymeningitis, p. 310—Internal pachymeningitis, p. 311—Acute spinal leptomeningitis, p. 312—Chronic spinal leptomeningitis, p. 316—Multiple sclerosis, p. 317—Subacute cord degeneration, p. 322—Syringomyelia, p. 324—Muscular dystrophies, p. 331.

### PROGRESSIVE MUSCULAR ATROPHY

Progressive muscular atrophy is a very comprehensive term. It may denote a symptom; it may denote an idiopathic condition; it may be the result of central or peripheral causes. Many writers regard it as synonymous with amyotrophic lateral sclerosis. There are, no doubt, many instances in which autopsies prove that the two diseases are closely allied. On the other hand, many autopsies have proved that the two are separate entities. Therefore, it is not easy to describe the condition unless one assumes a more or less arbitrary position.

Under this heading the writer will describe progressive muscular atrophy as an entity and will take the position that as such it is purely of central origin. In these instances it is best to assume that the progressive muscular atrophy of central origin is of two kinds: (1) spinal, and (2) bulbar. The words *spinal* and *bulbar* should be regarded merely as qualifying adjectives, denoting distribution rather than differentiation. The spinal type is the more common; the bulbar type is rare. The process often begins in the spinal cord and extends to the bulb. The latter type, therefore, may appear as the advanced stage of the spinal type, as the terminal stage of the amyotrophic lateral sclerotic type, or it may be limited to the bulb.

The pathology of the conditions is identical in the bulbar, the spinal, and the complicating types, regardless of whether the location is high up in the bulb, low down in the cord, or disseminated throughout the cerebrospinal axis.

**Etiology.**—The cause of progressive muscular atrophy is obscure. The factors which are considered are syphilis, heredity, overexertion and trauma. The condition occurs in young adults and especially among those subject to hard labor.

**Symptomatology.**—The symptomatology varies according to the part

of the central nervous system involved. Therefore, the clinical course and special symptoms of these conditions will be considered separately.

**CLINICAL COURSE.**—All forms begin insidiously and develop slowly. Months, or even years, may elapse from the appearance of the first symptom to the full development of the condition. Weakness and muscular wasting mark the beginning; loss of function and partial paralysis soon follow; complete paralysis and death mark the termination. The process is slow and may stop at any time; it may be characterized by a series of remissions or exacerbations. The patient suffers no pain, but increasing loss of function.

**SPECIAL SYMPTOMS OF SPINAL TYPE.**—In the spinal type the small muscles of the hand are the first to weaken and waste. The patient notices an inability to use the thumb and fingers; fine movements are performed with lack of skill and with clumsiness. A loss of substance gradually appears in the thenar and hypothenar eminences, and in the interossei. The hand assumes a claw-like attitude, which is typical and pathognomonic of this condition. The process may not extend further, or, as is more common, it may involve parts of the forearm and later the arm and shoulder. It is usual for particular groups of muscles to be affected, but not necessarily adjoining muscles. It is more usual for the shoulder muscles to atrophy after those of the arm, and following this, those of the neck and back. Later on, as the disease advances, it may attack the hip or trunk muscles, but rarely those of the legs. When the head and neck muscles become affected, the head drops upon the chest and the patient stoops. The face may even waste. The affected muscles show fibrillary twitchings and delayed response to the electric current. The reaction to the faradic current is either delayed or absent, and to the galvanic current it is changed, so that the muscular reaction is greater to the positive poles than to the negative. This is known as the reaction of degeneration.

**Objective Symptoms of Spinal Type.**—The objective symptoms are (1) atrophy, (2) fibrillary twitchings, (3) paralysis, (4) reaction of degeneration, (5) changes in reflexes, (6) deformity and changed attitude.

**Atrophy** is the most important symptom. To its presence the disease owes its name. It is the first to attack the patient, although not necessarily the first to arrest his attention. Its character is that of a simple wasting, its nature slowly progressive, and its distribution somewhat characteristic. The hand is the member first attacked. The small muscles become atrophied, especially the interossei and the muscles of the thumb. This is evident by a flattened appearance of the hand and a sinking of the interosseous spaces.

Months or even years may elapse before the atrophy shows marked progress. It advances by jumps and does not necessarily attack adjacent muscles. From the hand it may pass over the forearm muscles and next attack the deltoid, and may then affect the muscles of the back. There is no uniformity of involvement; it may even appear simultaneously in several places. The favorite places to be attacked are

the hands, arms, shoulders and back. The muscles of the face and neck are often involved, rarely those of the leg. As the atrophy is slow to advance, it follows that the patient has opportunities to adjust himself to his changed condition. Other and adjacent muscles are brought into play. The wasting, therefore, is not observed, and the patient calls attention first of all not to the atrophy but to the loss of function.

*Fibrillary twitchings* invariably accompany muscular atrophy of central origin. They may even precede the atrophy and be the first signal of the approaching disease. They can be elicited by lightly tapping the muscle. It should never be forgotten that fibrillary twitchings occur in many other conditions.

*The paralysis* is the result of the atrophy, but often is the first symptom to attract the patient's attention. This is partly due to the slow progress of the atrophy and to the patient's ability to make amends for the beginning loss of function. The paralysis is first evidenced by an inability to perform certain simple functions, such as eating, dressing, and writing. Later there is complete loss of power of the hand, arm and forearm.

*The reaction of degeneration* is present in the markedly wasted muscles, a partial reaction in those less atrophied, and a diminution of excitability to the electric current in those just beginning to be affected.

*The changes in the deep reflexes* are distinct, definite, and constant. They are diminished or absent, according to the extent and distribution of the atrophy. In those cases in which the reflexes are exaggerated the case should not be considered as one of pure muscular atrophy, but rather one of amyotrophic lateral sclerosis.

*The deformities* may be numerous and depend upon the distribution of the atrophy. The characteristic deformity is that of the *claw-hand*, or *main en griffe*. This is due to the frequency with which the disease attacks the hand.

*The attitudes* of dropped hand, of sloping shoulder, or of drooping head, are also the direct result of the paralysis. So gradual, however, may be the latter that the changed attitude may be evident before the wasting.

*Subjective Symptoms of Spinal Type.*—The subjective symptoms are weakness, impaired function, and clumsiness.

*Weakness*, resulting in muscular atrophy, is often the first symptom to attract the patient's attention. It occurs in the fingers and hands. The patient notices difficulty in dressing and in eating. Later he notices increasing difficulty in raising the arms and in lifting, carrying, and grasping.

The patient may complain of *impaired function*. He may observe an inability to perform his usual functions or to do his regular work.

*Clumsiness* is noted early by the patient. It is apparent in the finest movements of the fingers and hands.

*SPECIAL SYMPTOMS OF THE BULBAR TYPE.*—In the bulbar type the disease attacks the muscles which control the acts of speaking, swallowing, whistling and the like. This type is terminal, and usually appears

state in the disease. The symptoms are the usual ones of bulbar paralysis: difficulty in swallowing, nasal regurgitation, nasal speech, inability to pronounce the labials and linguals, and stiffness of the tongue.

**PHYSICAL EXAMINATION.**—The physical findings determined by observation are those of atrophy, weakness, deformity and partial paralysis. *Special tests* show very little. They are of aid from a negative rather than a positive point of view. The exception is the presence of fibrillations in the strands of the affected muscles, the absence of reflexes and, in the bulbar type, the inability to eat and talk.

**LABORATORY FINDINGS.**—Laboratory analyses are of no avail.

**SPECIAL EXAMINATIONS.**—An electrical examination will show changes or the presence of the reaction of degeneration. There will be delay or absence of response to both faradic and galvanic currents or the reaction from the positive pole will be greater than from the negative.

**Diagnosis.**—The diagnosis is made on the clinical history of weakness and wasting of the muscles which occur in young persons who have been used to hard labor. The wasting is apt to begin in the small muscles of the hands. To these main facts must be added the absence of any positive laboratory findings, the loss of the knee-jerk, the loss of electrical reactions, the presence of fibrillary twitchings and a claw-like appearance of the hand.

**DIFFERENTIAL DIAGNOSIS.**—Progressive muscular atrophy is to be differentiated from five other conditions: syringomyelia, anterior poliomyelitis, amyotrophic lateral sclerosis, lead paralysis, and caries of the vertebræ. The main differences can be described in a few words.

In *syringomyelia* occur the typical sensory changes, the spastic paraplegia, the trophic changes, and the unilateral location of the atrophy.

In *chronic anterior poliomyelitis* there is a rapid onset, loss of power before atrophy and a different distribution.

In *amyotrophic lateral sclerosis* there is spasticity with exaggerated reflexes illustrating a rigid type of paralysis.

In *lead paralysis* occur the colic, the blue lines on the mucous membranes, the extensor paralysis, and the presence of lead in the urine.

In *caries of the vertebræ* there are sensory symptoms, sphincter involvement, pain, and usually a positive x-ray finding.

**Treatment.**—The treatment of progressive muscular atrophy may be divided into (1) general treatment and (2) symptomatic treatment.

*The general treatment* consists of attention to the general laws of hygiene. These patients need a great deal of rest, air and sunshine. Tepid baths relieve the muscular fatigue. Nourishing foods, and especially those which are fat-producing, are indicated. Beef juice and cod-liver oil are the best adjuvants.

*The symptomatic treatment* consists largely of tonics and cathartics. Nitrate of strychnia in 1/40 grain (0.00162 gram) doses should be given from time to time and then stopped. The hypodermic administration is sometimes of value.

**Prognosis.**—The prognosis as to recovery of function is bad. These patients generally live for years. The condition may become arrested at

any period or may start anew. The mode of death is from an intercurrent condition. These patients have lowered resistance and usually succumb to pulmonary affections or fall victims to any prevailing epidemic.

**Pathology.**—The pathological lesion is situated in the gray anterior horns. Accompanying changes may occur in the anterolateral columns and pyramidal tracts, but the essential and characteristic change occurs in the gray anterior columns. The nature of this lesion is an atrophy which is widespread and complete; it involves both nerve-cells and fibers and affects anterior roots, motor nerves, and muscles. The nerve-cells shrivel up, their processes disappear, and their nuclei become indistinct. At first only a few cells are affected. As the condition advances, the entire anterior horn may degenerate and even disappear. Upon autopsy the muscles appear small and wasted and of a pale or yellowish color. A microscopical examination of the affected muscles reveals nothing beyond simple atrophy. In some cases the fibers show evidences of degeneration, together with a loss of the transverse striation; in others, the fibers show degeneration together with absorption, so that nothing remains but the muscle sheaths. There are cases in which the muscle fibers have not only lost the typical transverse striation but, in addition, have a longitudinal striation. There may also be an increase of interstitial fibrous tissue.

## MYELITIS

The term myelitis may be applied to three classes of cases:

1. Those which present the symptoms of myelitis as the result of an acute process—*acute myelitis*.
2. Those which present the symptoms of myelitis as the result of a mechanical compression of the spinal cord—*compression myelitis*.
3. Those which present the symptoms of myelitis in a chronic and well-established form as the result of either acute or compression myelitis—*chronic myelitis*.

### 1. ACUTE MYELITIS

**Etiology.**—The predisposing causes of acute myelitis are often obscure. Exposure to wet and cold have undoubtedly precipitated some cases. Season, altitude, soil, sex, and race are not factors. Many cases develop in young persons of both sexes. Neither personal nor social conditions influence its cause. It has followed trauma, especially blows on the back. In rare cases muscular overexertion and strain have precipitated myelitis. It has occurred following septic infections, gonorrhea and syphilis. It often follows childbirth; in this instance it may be septic. Neither heredity, personal condition, nor environment are factors in its origin.

Myelitis most frequently follows the acute infectious diseases—typhoid, typhus, malaria, influenza, and small-pox. Tuberculosis has been reported as the cause in some instances. In many cases the patient suddenly develops fever, which is followed by myelitis.

Acute myelitis may then be caused by a toxic condition, a true inflammatory condition, or by an acute degeneration, the result of some circulatory disturbance in the vessels of the spinal cord.

**Symptomatology.**—**CLINICAL HISTORY.**—*Mode of Onset.*—*Symptoms during the Progress of Disease.*—Acute myelitis has a sudden and rapid onset. There is headache, malaise, shivering or a chill, followed by a rapid rise of temperature. The patient complains of dullness, nausea, and tingling in the ankles and feet. Weakness and heaviness develop in the legs. The bladder ceases to function; there may be retention or dribbling. This stage lasts only three or four days. The acute symptoms subside, the fever abates, and the patient at once begins to feel better. It is then that the symptoms which are characteristic of all three types of myelitis become well pronounced. The legs and sphincters are paralyzed. There are anesthesia, rigidity, and exaggerated reflexes. These symptoms vary according to the severity of the infection, the extent of the pathological process and the portion of the spinal cord which has been attacked. The patient convalesces slowly and gradually, and the condition becomes chronic.

*Objective Symptoms.*—The objective symptoms are: fever, paralysis, spasticity, changes in reflexes, trophic disturbances and atrophy.

The fever in acute myelitis lasts only a few days. It rises on the first day to 103° or 104° F. (39.4° or 40° C.) and at the end of three or four days drops to normal. There are no great variations between morning and evening curves.

*Paralysis* is rapid in onset, reaching its height in a short time. At first it is flaccid, later spastic. The legs are more frequently affected than the arms.

*Spasticity* develops except where the lesion is complete. Both legs are stiff, the reflexes are exaggerated, and the gait spastic.

The reflexes are at first lost; later they become exaggerated. This is especially true if the lesion is in the dorsal region. Both ankle clonus and Babinski's reflex are present.

*Trophic disturbances* in the form of bed-sores over the sacrum and heel are frequent, as the disease advances.

*Marked atrophy* in the paralyzed limbs develops. It is an atrophy of disuse; in a few instances where the cells of the anterior horns have been invaded it is central in origin.

*Subjective Symptoms.*—The subjective symptoms are: malaise, pain, weakness, tingling and heaviness in the legs, sphincter involvement and sensory disturbances.

*Malaise* ushers in the disease. It lasts a few hours and resembles that seen in all acute conditions.

*Pain* is often present. It is dull in character, short in duration, and distributed to the back. It does not occur in the vertebrae.

*Weakness* is one of the first symptoms noted by the patient. It becomes less general as the condition advances and is referred to the legs.

*Tingling in the legs* is an early symptom. In a few days it passes, giving way to heaviness.

Both *sphincters* are usually affected. The bladder symptoms may be those of retention or leakage. The most common type is dribbling, resulting from overdistention. The urine becomes alkaline; cystitis almost invariably develops. Paralysis of the bladder may precede that of the legs.

The *sensory disturbances* vary from slight impairment of touch and pain to complete anesthesia. This variation is dependent upon the extent, severity, and location of the lesion. The upper level of the anesthesia is marked by a band of hyperesthesia.

**PHYSICAL EXAMINATION.**—The physical findings determined by observation are those of a patient acutely sick with temperature, pain, paralysis of the legs and arms, together with an involvement of the sphincters. *Palpation* reveals some tenderness of the muscles and a distended bladder. The *special tests* show the presence of exaggerated reflexes, loss of sensation, more or less complete, extending up to the level of the lesion, and an area of hyperesthesia just above that level. The exaggeration of the reflexes varies according to the stage and location of the disease and the type of the infection.

**THE LABORATORY FINDINGS.**—In acute myelitis the laboratory findings throw no light on the cause or progress of the disease. There may be a slight degree of anemia in the blood, and a trace of albumin in the urine. The spinal fluid is negative.

**SPECIAL EXAMINATIONS.**—Special examinations do not help in the diagnosis of acute myelitis. Neither functional tests nor instrumental examinations are of value. The *x-ray* is only of service where the myelitis is caused by new growths, fractures, dislocations, or caries. As none of these conditions enter into the causes of acute myelitis, the *x-ray* is directly of no help. It does indicate, in the secondary or compression type of myelitis, the existence of a definite cause.

**Diagnosis.**—The diagnosis of acute myelitis is made on the clinical history of a short, severe, and rapid infection, with high temperature; on the physical finding of a spastic paraplegia with loss of power, loss of sensation, and loss of sphincter control; and on the absence of laboratory findings and special examinations. The important points in the diagnosis are the absence of a mechanical cause for the paralysis, and the presence of a sudden infection. In every case of suspected myelitis it is most important to examine the back.

**Complications.**—The complications of myelitis are twofold: (1) those which may occur in any spinal cord condition; and (2) those which may result from the location of the particular pathological lesion. Of the former, the most common are pneumonia, exhaustion, toxic psychoses, bronchitis, cardiac conditions—both valvular and muscular—and the results of infectious processes. Of the latter, the most common are bed-sores, cystitis, pyelitis, nephritis and paralysis of the intercostal muscles and diaphragm.

**Sequels.**—Acute myelitis follows one of three courses: the patient either recovers, develops chronic myelitis, or dies. The sequelae, there-



fore, are the symptoms of chronic myelitis, namely, paralysis, rigidity, sphincter involvement, bed-sores, etc.

**Association with Other Diseases.**—Acute myelitis is not infrequently associated with childbirth. It follows the infectious diseases. In some cases it occurs with gonorrhea and in some cases with general sepsis. In those instances in which the cause is toxic, it is of course associated with the original cause of the toxemia, being in itself a secondary condition. Whether the myelitis occurring in parturition is septic in origin is still an open question. Syphilis and tuberculosis are occasionally complicated by acute myelitis. In these instances the acute condition may originate from an entirely different cause, such as exposure to wet and cold, trauma, or an additional infection. It may even be associated with the simplest type of infection, such as a septic tonsil, whitlow, or even a septic tooth, or it may follow the administration of salvarsan.

**Clinical Varieties.**—The clinical varieties are: (1) cervical; (2) dorsal; (3) lumbar or lumbosacral; (4) transverse—complete and incomplete; (5) disseminated; and (6) acute central.

(1) **CERVICAL MYELITIS.**—In this form of myelitis the lesion is in the cervical region. Paralysis, anesthesia, and oculopupillary symptoms are present, plus the ordinary symptoms of dorsal myelitis. If the lesion is situated very high in the cervical region, the arms are rigid; if low down, flaccid and atrophic. The legs are always rigid, and, therefore, illustrate a spastic paraplegia. The anesthesia involves the trunk and all four extremities. There may be dyspnea from an involvement of the intercostal muscles or the medulla. The diaphragm may be involved.

(2) **DORSAL MYELITIS.**—Dorsal myelitis is the most common type. This is so because the dorsal segment is the largest and has an inferior vascular supply. The symptoms are: paraplegia, anesthesia, exaggerated reflexes, sphincter paralysis and bed-sores.

The paraplegia, the anesthesia, and the condition of the reflexes and sphincters vary according to the extent and duration of the lesion. They may be slight or complete, so that the patient may be able to walk with slight loss of sensation, mildly exaggerated reflexes and partial loss of control of both sphincters, or he may, in an advanced case, be bedridden, with a complete spastic paraplegia, incontinence, and loss of sensation. The sphincters may show incontinence or retention; priapism may be present. Bed-sores occur over the bony prominences, at the sacrum, the trochanters and the heels. They are due to loss of sensation, pressure, and lack of cleanliness. Edema, lack of perspiration, and trophic disturbances may develop. There may be effusions into the large joints.

(3) **LUMBAR MYELITIS.**—In lumbar myelitis the symptoms are: atrophic paralysis, lost reflexes—both superficial and deep, reaction of degeneration, anesthesia, sphincter involvement and bed-sores.

The extent of these symptoms varies with the extent of the lesion. The upper level of the anesthesia marks the level of the lesion. In this form the feet are dropped and the legs extended.

(4) **TRANSVERSE MYELITIS.**—The symptoms are those of a transverse

lesion of the cord. If the lesion is complete, the paralysis will be complete.

(5) **DISSEMINATED MYELITIS.**—In this form the lesion is disseminated, the foci scattered. The latter may be many or few, situated in the cord, pons, medulla, or even in the optic nerves. The symptoms depend upon the location, number and extent of these foci. The usual train of symptoms consists of paralysis, anesthesia, sphincter involvement, reflex abnormality and bed-sores.

In this form of the disease, the symptoms vary as the condition changes and progresses.

(6) **ACUTE CENTRAL MYELITIS.**—This form of myelitis is rare. It is usually rapid, has the symptoms of an acute condition, and of that part of the spinal cord which happens to be involved.

**Treatment.**—**GENERAL MANAGEMENT.**—The treatment of myelitis is most important. Special attention should be given to the care of the patient, to the symptoms, and to the complications, especially those of the bladder. To avoid pressure and the formation of bed-sores the patient must lie on a **water-bed**. His position should be changed every few hours. The greatest possible attention must be devoted to the **skin**. **Alcohol sponging and rubbings** should be given and **talcum powder** used daily. The skin must be kept hard and free from pressure. The greatest possible cleanliness must be observed about the bed. **Wet sheets must be instantly removed, and the skin kept dry. Rings of gauze** should be placed under the sacrum and heels. If the proper precautions are observed, and careful and faithful nursing carried out, bed-sores can be avoided. There are some cases in which bed-sores are inevitable, but these are in the minority. If the skin becomes red or shows signs of breaking down, it should be washed with an astringent solution—**alum, tannin, or eau de cologne**. Once the bed-sore has formed, efforts should be made to prevent its extension, and to keep it clean. For these purposes the best remedies are **ointments of zinc, vaselin, or iodine**. In some cases **washing of the bed-sore with a bichlorid of mercury solution or other disinfectant will help**. For the chronic bed-sore, Williamson recommends **iodid of starch paste**. **Warm water** should be used to wash these sores.

A **high altitude and a dry climate** are best. If the patient needs expert nursing or catheterization, residence in a hospital is essential.

**Diet.**—The diet, while the fever lasts, should consist of milk. As soon as this subsides, the patient may take semi-solids, and then a regular diet may be resumed. The patient should have a proper proportion of proteins, carbohydrates, and fats. Beef-juice, eggs, cheese, bacon and cereals are especially good.

**VARIOUS FORMS OF THERAPY—MASSAGE.**—The various forms of therapy—hydrotherapy, radiumtherapy and mechanotherapy—are of no use. **Massage**, after the acute stage is passed, together with electricity, will help the wasted muscles, strengthen and encourage the patient. There is no proof, as yet, that any of the vaccines or sera are of benefit.

**TREATMENT OF COMPLICATIONS.**—The care of the bladder is equally

important. Constant examinations should be made to ascertain if the patient is emptying the bladder—the patient's word must never be taken. Dribbling of urine may indicate either a paralyzed or an overdistended bladder. It should never be forgotten that cystitis, pyelitis, pyelonephritis, and general sepsis may all follow an overdistended bladder. If cystitis is present, the bladder should be irrigated daily. The best solution to use is one of **boric acid**. **Urotropin**, 20 to 40 grains (1.3 to 2.6 grams) daily, should be given. The urine should be kept acid.

**SYMPTOMATIC TREATMENT.**—The painful contractions of the legs may be relieved by **warm baths**, **gentle massage with cocoa butter**, and with **passive movements**, or **small doses of the bromids**.

**MEDICINAL TREATMENT.**—Drugs should be used sparingly. If there is definite evidence of a distinct causative factor, such drugs are indicated as may be of value for the particular condition. Apart from this, the only ones of service are **laxatives and tonics**. **Calomel**, from time to time, and a **mild iron and strychnia tonic** are the best.

**Prognosis.**—**AS TO RECOVERY.**—Prognosis as to life is fairly good. The majority of patients live on, though a small number make a complete recovery. Few cases, however, fail to leave behind a long train of symptoms, with more or less paralysis. The prognosis is less favorable in the disseminated and in the dorsal forms. Recovery is probable in those cases which follow the infectious diseases and in those secondary to syphilis.

**MODE OF DEATH.**—Death results from bladder complications, pyelitis and cystitis, sepsis secondary to the bed-sores, paralysis of the diaphragm and intercostal muscles, and from intercurrent diseases, as pneumonia and bronchitis. In some cases the process ascends to the medulla, and death results rapidly from paralysis of the respiratory center.

**Pathology.**—**MACROSCOPIC.**—Upon autopsy, the cord appears softer in the affected region. The location of the myelitis is, therefore, easily discernible. Palpation corroborates this as the cord feels softer. A cross-section made of the diseased area will be found to be yellow or grayish-yellow; if the condition is more recent it may be reddish-yellow. There is blurring of the finer markings; the gray and white portions of the cord are not distinct, but merge into each other. There exists a condition of degeneration which may be so marked as to be evident to the naked eye.

The pathological processes in myelitis are threefold: degenerative, circulatory and proliferative. The changes vary, according to which factor predominates, and also according to which is the first to appear. The vessels may suffer first and be the cause of degenerative changes in the tissues, or the tissues may undergo changes and act upon the vessels.

**MICROSCOPIC.**—The microscopical examination reveals one or many foci of inflammation. If degeneration predominates, the axis cylinders and myeline sheaths are swollen, the vesicular spaces are filled with granular cells, fatty detritus, swollen glia and decomposed cells. If the predominating disturbance is circulatory, there are vascular dilatation, swelling, edema, small-celled infiltration, minute hemorrhages, and softening.

The process, therefore, is one of disintegration, degeneration, necrosis and softening. Oppenheim says the process may appear in one of three forms—a vesicular condition, a focus of softening, or in the form of cicatricial foci.

## 2. COMPRESSION MYELITIS

Compression myelitis is synonymous with compression of the spinal cord. It is a term applied to those changes in the spinal cord which result from several diseases. In some instances, the compression is primary from the original lesion, in others, secondary.

**Etiology.**—The causes of compression myelitis are: tubercular diseases of the vertebræ, tumors of the spinal cord, syphilis, aneurysms, bony hypertrophies, malignant growths, meningeal disease, fracture and dislocation of the vertebræ and abscess.

Each one of these conditions is progressive and produces a slow compression of the membranes, vessels, tracts, nerve-roots and of the spinal cord itself.

**Symptomatology.**—**CLINICAL HISTORY.**—The clinical history of compression myelitis is one which is long, slow and gradual. It begins with few symptoms, and terminates with many. The nature of the symptoms and the course of the disease are wholly dependent upon the original condition causing the compression. Thus, the mode of onset, if resulting from a slowly growing aneurysm, may be gradual; if resulting from a rapidly growing spinal cord tumor, may be rapid.

**Objective Symptoms.**—The objective symptoms are numerous: paralysis, stiffness, deformity, spastic gait, changes in reflexes, atrophy, trophic changes and electrical changes.

The *paralysis* begins as motor weakness and gradually extends to complete paraplegia, with the attendant symptoms of stiffness, exaggerated reflexes, and loss of sensation.

The *stiffness* is most evident in those cases resulting from tubercular disease and tumor of the spinal cord. The muscles of the extremities become spastic, according to the location of the lesion.

*Deformities* occur in cases of bone involvement, in tubercular and traumatic cases. They may assume any one of the many forms of spinal curvature, or simply appear as a displaced knuckle in fracture-dislocation cases.

*Spastic gait* is an invariable symptom of spinal cord compression. It occurs in the early stages, before the lesion is complete. It may vary from a slight stiffness and stubbing of the toes to a typical spasticity, with scraping, shuffling, and stiffness.

The *changes in reflexes* in compression myelitis are of two kinds: (1) in the early stages the reflexes are exaggerated, due to irritation; (2) in the terminal stages they are diminished and later lost, due to destruction and complete cutting off of impulses. These two types of reflex changes are especially evident in tumors of the spinal cord where the disease is steadily progressive and the attendant physical changes vari-

able. The reflexes at the level of the lesion may differ from those below the level.

*Atrophy* is present in those instances in which there is an involvement of the anterior horns.

*Trophic disturbances* in the form of bed-sores occur in spinal cord tumors where the lesion has invaded the anterior horns.

*Electrical changes* vary from slight loss of faradism and galvanism to a complete reaction of degeneration. They occur together with atrophy and trophic disturbances.

*Subjective Symptoms.*—The subjective symptoms are: pain, tenderness on motion, sensory changes and sphincter disturbances.

*Pain* is frequent. It may be neuralgic and shooting in character, or deep and boring. It may result from pressure on a plexus or on an individual nerve, or it may result from root involvement. It is usually unilateral, but may be bilateral. In rare cases of spinal cord tumor pain is absent. In tubercular cases it occurs in the back.

*Tenderness* on motion is especially evident in tubercular cases and where bone is involved. It may also be present in traumatic cases.

*Sensory changes* in compression myelitis are constant and important. They vary from slight disturbances to complete loss of sensation to touch, pain, heat and cold. These sensory changes vary according to the site and location of the lesion. There may be irritative changes at and above the level of the lesion, with destructive changes and anesthesia below the level of the lesion. If the cause of the compression affects one side more than the other a dissociation of anesthesia presents itself, with loss of pain and temperature sense on the opposite side, and loss of deep sensibility on the same side—a phenomenon called the Brown-Séquard symptom complex.

The Brown-Séquard syndrome is the name given to conditions of unilateral transverse division of the cord, whether due to trauma or compression. The clinical picture which presents itself is that of a motor paralysis, hyperesthesia to touch, paralysis of deep sensibility and vasomotor changes on the same side as the lesion, with loss of pain and temperature sense on the opposite side. This more often is atypical, as the lesion is seldom complete.

*Sphincter disturbances* will be present if the compression is marked and occurs at or above the centers for sphincter control.

**PHYSICAL EXAMINATION.**—Examination reveals a patient more or less paralyzed, with a beginning spastic gait, stiffness and pain. *Palpation* may show a sensitive spinal column, a deformity, or a bulging near the vertebræ. *Percussion* in the examination of compression myelitis is not of very great value. It sometimes will reveal a sensitive vertebra in cases of spinal caries, and sometimes it may show the presence of a tumor. *Auscultation* is of course of no value. *The special tests* show exaggerated or lost reflexes and an abnormal gait.

**LABORATORY FINDINGS.**—The laboratory findings are numerous. In specific cases, the spinal fluid will establish the diagnosis by the presence of a Wassermann reaction, a high cell count, a plus globulin reaction, and

a huetic curve. In spinal cord tumors, as a result of long compression, the fluid will sometimes be yellow in the distal part below the tumor, due to the disintegration of the red blood-cells. This is called xanthochromia. In irritative conditions arising from meningitis, there is a pleocytosis of the spinal fluid. In tuberculous conditions, a lymphocytosis is frequent.

**Diagnosis.**—The diagnosis of compression myelitis is made from the clinical history of a slowly advancing paralysis of the lower or upper extremities, together with a considerable amount of pain. When to these are added the laboratory findings given above, or the typical straw-colored fluid, and the physical findings of a spastic paraplegia, the diagnosis is a simple matter.

**Complications.**—The complications of compression myelitis are those of the original disease. It may be associated with many conditions, such as tuberculosis, osteomyelitis, cancerous conditions, specific and traumatic conditions.

**Clinical Varieties.**—The clinical varieties of compression myelitis may be divided into two classes: (1) the complete; (2) the incomplete.

**Treatment.**—**PROPHYLACTIC TREATMENT.**—**Early diagnosis** is the prophylactic treatment of compression myelitis. The early detection of any one of the causes producing compression myelitis may warrant action to arrest the pressure, and so prevent further damage. Thus, a cyst or tumor may be removed, a tubercular condition treated, a deformity corrected.

**GENERAL MANAGEMENT.**—The general management of the patient is most important. He should have **complete and prolonged rest**; the way to secure this is to keep the patient in bed for a long period of time—weeks or months. The bed should be what is known as a **water-bed**. The best **climate** is one that is **dry, cold and stimulating**. **Sunshine** is of great help.

**Diet.**—The diet should be abundant and nutritious. Fat-producing foods and beef juice give the best results. These patients should be made to eat large amounts, and especially to eat cheese, butter, eggs, and to drink cream and milk. These latter factors of diet and climate are of especial importance when the cause is tuberculous. The bed may be wheeled out of doors on bright days.

**LOCAL TREATMENT.**—Local treatment should be directed towards securing rest, or extension to the vertebral column. These may take the form of **plaster jackets, weights for suspension, sandbags** to prevent motion, and various **harnesses** for purposes of suspension, immobilization, or extension. **Prolonged rest** should precede the employment of these mechanical measures.

**SYMPTOMATIC TREATMENT.**—The treatment of symptoms embraces the care of the skin, the bladder, and the muscles. To care for the *skin* properly requires **cleanliness, friction, powders, lotions and alcoholic rubs**. The patient should have **rings for the heels and sacrum**. The *bladder* must be safeguarded against infection resulting from the constant use of the catheter and the presence of residual urine. If *cystitis*

occurs, **irrigations** and **urotropin**, 5 grains (0.324 gram), three times a day, is the best treatment. The *muscles of the legs* may be spastic or flaccid; great restlessness may annoy the patient. If the legs become spastic, little can be done other than **warm baths**; if flaccid, **electricity** will help. For the *muscular twitching*, Starr suggests 10 grains (0.65 gram) of **sodium bromid** every two hours.

**HYDROTHERAPY.**—Hydrotherapy can be used in moderation. Warm baths will quiet the patient, cold baths will stimulate him. They should be used as the conditions warrant.

**MASSAGE.**—Massage is beneficial to the paralyzed limbs after the acute stage. Passive movements may sometimes be of value.

**X-RAY AND RADIUM THERAPY.**—X-ray therapy is of little value. It may be used in those cases in which a malignant growth is suspected. Radium therapy can be placed under the same category. Both are of especial value in those cases in which it has been impossible to remove the entire tumor during the operation. Their application is thought to prevent a recurrence.

There is nothing to be gained by use of any of the other therapies.

**MEDICINAL TREATMENT.**—Drugs must be used sparingly and as secondary measures. The best are **general tonics**, containing **iron**, the various **phosphate preparations**, **arsenic**, **laxatives**, and **antiseptics for the cystitis**.

**SURGICAL TREATMENT.**—The surgical procedures are **laminectomy**, **tenotomy**, and **posterior nerve-root section**. Laminectomy is contraindicated in tubercular conditions, in others it may help. It must be avoided unless there are positive indications, such as removal of new growths or diseased conditions. Tenotomy will help when there exists a marked contraction of the calf muscles. Posterior root section may be resorted to when the spasticity has become permanent, contractures have developed, or the comfort of the patient has been seriously interfered with.

None of these surgical measures should be resorted to in haste. Rest in bed is all important. The presence of an abscess may call for curetting, draining, and further opening. The convalescence is slow and long drawn out. Its successful management calls for tact, patience and perseverance.

**Prognosis.**—The prognosis is of course dependent upon the cause. Tubercular conditions are always very serious. If not too far advanced, a degree of recovery may be brought about by the use of jackets and braces to immobilize the vertebral column. In tumors, if not malignant and not too deeply situated, surgery offers considerable aid. In syphilitic meningitis the proper treatment will arrest the process and cause great amelioration of the symptoms.

Those cases which develop a complete transverse myelitis with bed-sores, cystitis, and an involvement of the sphincters are the least favorable. Aneurysms and malignant growths hold out no hope.

**Pathology.**—The pathology of compression myelitis is of course dependent upon the original cause of the mechanical compression. It is

not possible in an article of this character to describe it at length. It is sufficient to mention the pathological condition which occurs in the most common cause—tubercular disease of the vertebræ. In this instance, the body of the vertebræ, as well as the laminae, may be invaded by a process which degenerates and forms pus. The bony mass of vertebræ softens, fails to support the arches above, and causes the typical deformity of Pott's disease. The microscopical examination shows inflammation, degeneration, and disappearance of the nerve elements. The axis cylinders swell, and there is a formation of new gliomatous tissue.

### 3. CHRONIC MYELITIS

**Etiology.**—Chronic myelitis should be regarded as the terminal stage of either acute or compression myelitis.

**Symptomatology.**—**CLINICAL HISTORY.**—The clinical history would, therefore, begin with the original cause and end with the arrested symptoms of a confirmed and well-established case of either acute or compression myelitis. The *onset* is gradual, the *course* slow, and the *duration* long.

**Objective Symptoms.**—The objective symptoms are paralysis, spasticity, changes in reflexes and trophic disturbances.

The *paralysis* is more or less complete and most frequently of the spastic type. There are rare instances in which there is an involvement of the cells of the anterior horns, giving rise to the flaccid type.

*Spasticity* is common. It may be slight or severe, showing a typical condition of spastic paraplegia.

The *reflexes* are exaggerated in the spastic type and absent in the flaccid.

*Trophic disturbances* consist of bed-sores, edema and blisters.

**Subjective Symptoms.**—The subjective symptoms are pain, weakness, loss of use of the legs and arms, heaviness in the legs, sensory disturbances, and sphincter involvement.

*Pain* is neither frequent nor severe. It occurs most often as a result of contractures or of stiffness. Sometimes it is sharp and shooting in character, similar to that in tabes.

*Weakness* is constant and distressing. It is both local and constitutional.

The *loss of the use of the arms and legs* is gradual and progressive. The patient may often complain of weakness before paralysis is evident.

*Heaviness in the legs* is constant. There is a sensation of great weight and inability to raise the legs when walking. The patient appears to push the legs.

The *sensory disturbances* are variable. They may consist of paresthesiæ or spots of anesthesia.

The *sphincters* are involved if the process is high up or advanced.

**PHYSICAL EXAMINATION.**—The physical findings are those of a chronic paralytic. The patient appears sick, is weak and stiff, and



moves with difficulty. Special tests show exaggerated or lost reflexes and slight sensory disturbances. The sphincters are affected.

**LABORATORY FINDINGS.**—The laboratory tests may show signs of specific involvement.

**X-RAY EXAMINATION.**—The x-ray, in traumatic or tubercular cases, shows definite changes.

**Diagnosis.**—The diagnosis is made on the previous history of an acute illness or of a compression of the cord.

**Complications.**—The complications are those common to chronic spinal cord conditions—bed-sores, cystitis, pyelitis, nephritis, sepsis and exhaustion.

**Sequelæ.**—Chronic myelitis, dependent on its original cause, advances more or less slowly. It is usually an arrested process. The patient dies from an intercurrent disease.

**Clinical Varieties.**—The clinical varieties are similar to those described in acute myelitis.

**Treatment.**—The treatment is similar to that of any chronic spinal cord disease. Either the original cause or the symptoms may call for treatment. The reader is referred to the treatment of the other spinal cord conditions.

**Prognosis.**—The prognosis in chronic myelitis, so far as life is concerned, is good; so far as cure is concerned, it is dependent upon the cause.

**Pathology.**—The pathological changes occurring in chronic myelitis, are those of sclerosis and degeneration. The sclerosis is distributed irregularly in both gray and white matter; the degeneration is of both nerve-cells and fibers; it, too, is irregular in distribution.

**Historical Summary.**—In olden times the conception of myelitis was very comprehensive, embracing degenerative and sclerotic processes. As late as 1897 Virchow referred to this older view of inflammation based on anatomical classification. In 1887 Pierre-Marie pointed out that the factor of prime importance in myelitis was the genesis of the disease, not the anatomical change. As a result, many observers studied the production of artificial myelitis. Chemicals and pathogenic organisms were used. The route of introduction was both the intravenous and the intraspinal. As our knowledge of spinal cord conditions has advanced, our conception of myelitis has changed and become more restricted.

### AMYOTROPHIC LATERAL SCLEROSIS

**Etiology.**—The cause of amyotrophic lateral sclerosis is not known. No predisposing cause exists. Neither cold, climate, season, nor altitude has any bearing on the disease. In origin, it is neither bacterial nor toxic. The sexes seem to be equally divided, although it is more often seen among women. Heredity is a factor in its development. The most reasonable assumption is that in most cases there exists, from birth, a congenital weakness of the entire motor system. The cause is not in-

fluenced by occupation, trauma, nor overexertion. It is not associated with other diseases, and it does not necessarily follow the infectious diseases. It is, like most degenerative conditions of the nervous system, a disease of early life. The majority of cases occur between twenty and thirty-five years of age.

**Symptomatology.**—CLINICAL HISTORY.—*Mode of Onset—Symptoms during Progress of Disease.*—There is no period of incubation in amyotrophic lateral sclerosis. The onset is gradual, extending over a period of months. The first symptoms are weakness, atrophy and rigidity. The condition usually begins with weakness and atrophy of the hands. The muscles affected are those of the thenar and hypothenar eminences, and the interossei.

Shortly after the appearance of the atrophy, rigidity develops in the legs. The two conditions of atrophy and rigidity then go hand in hand. The rigidity advances upwards, until finally it involves not only the legs but also the arms. The weakness and atrophy simultaneously advance upward, so that eventually they involve the muscles of the shoulder and neck. The arms and legs, by this time, are completely paralyzed and rigid. Below the waist the patient presents the syndrome of spastic paraplegia; above the waist, the syndrome of flaccid paraplegia. Later both atrophy and rigidity become general. In its early stage the disease thus presents two distinct clinical pictures: (1) of the lower extremities, in which the pathological involvement is of the upper motor neurons, and (2) of the upper extremities in which the pathological involvement is of the lower motor neurons. The condition advances slowly, may at any time remain stationary, but, as is more usual, goes on to the third stage. This third stage consists of an involvement of the nuclei of the bulb or glossolabiolaryngeal paralysis. The speech is slow and monotonous, the lips are atrophied, and the patient notes difficulty in swallowing. The muscles of the lower part of the face and the laryngeal muscles waste, so that the patient presents a pitiful appearance. Voluntary actions, like whistling and talking, are impossible. The mind becomes feeble, and the patient emotional and childlike. Paralysis of the respiratory muscles renders breathing difficult. Finally, death follows from either respiratory failure or foreign body pneumonia.

The picture just drawn is the usual one. The development of the disease may vary—that is, the rigidity of the legs may appear first, to be followed by the atrophy of the arms, or the two may go hand in hand. The bulbar symptoms rarely inaugurate the condition, but often terminate it.

*Objective Symptoms.*—The objective symptoms are: atrophy, rigidity, exaggeration of the reflexes, fibrillary twitchings, spastic gait, bulbar symptoms, electrical reactions, paralysis and mental disturbances.

The *atrophy* may begin in either the arms or legs; its usual site is the small muscles of the hands, the thenar and hypothenar eminences, and the interossei. It then involves the arm and forearm. Later, it may involve the legs. The advance may be slow or rapid, varying in pro-

portion to the severity of the case. The type of the atrophy and its course resemble progressive muscular atrophy.

*The rigidity* attacks both trunk and extremities. It follows the appearance of the atrophy and, beginning in the legs, later ascends to the trunk, arms, neck and sometimes the head. In the legs it becomes very marked, giving rise to spastic paraplegia. The legs become stone-like, locked, and immovable. Clonus may be elicited.

*The reflexes* are markedly increased. There is an exaggeration of the knee-jerk, the tendo achillis reflex, the plantar, and in fact of all the reflexes. Beevor says that the exaggeration of the jaw-jerk, with resultant clonus, is diagnostic of the disease.

*Fibrillary twitchings* may be elicited by tapping the atrophied muscles. They appear early, often before the atrophy is evident.

*The gait* early shows symptoms of spasticity, stiffness, shuffling and scraping. It steadily progresses and eventually terminates in complete paralysis.

*Bulbar symptoms* are a late and terminal manifestation. In rare cases they inaugurate the disease. They consist of the usual slow, nasal speech, the atrophied lips and tongue, and the difficulty in swallowing and chewing. The muscles of the face atrophy, droop, and finally the patient cannot speak.

*The electrical examination* is always pathological. It varies from a slight diminution to both faradism and galvanism, to a complete reaction of degeneration.

*Paralysis* begins with a slight impairment of the arms, then of the legs, and finally involves the entire body. If the disease is of long duration, it may become complete and general. The writer has seen cases in which the patient was able to move only the head, the rest of the body being atrophied and rigid.

*The mental symptoms* consist of emotional disturbances and childishness. Towards the end there is a distinct enfeeblement of the higher faculties.

*Subjective Symptoms.*—The subjective symptoms of amyotrophic lateral sclerosis are muscular weakness, impaired function, pain, stiffness, loss of power, speech fatigue and difficulty in swallowing.

*The muscular weakness* involves both trunk and extremities. It begins in a very slight form, and progresses to complete paralysis. It is first noticed in the hands, then the arms, and later in the legs. It may, however, begin in the legs.

*The failure of the hands to perform their usual functions* is often the first symptom of the disease. The patient notices that he cannot hold a pencil, cannot button his clothes, or cannot feed himself as well as usual. The hands, and especially the fingers, become weak; there is no ataxia, and rarely numbness.

*Pain* is neither frequent nor constant. It may occur in the arms or legs as a result of the weakness or the rigid and fixed position. Williamson says it may be present in the neck.

The patient complains of *stiffness in the legs*, which appears shortly

after the atrophy in the arms. It advances steadily and may later involve the arms and trunk. It may become very marked and be the cause of great discomfort.

*Loss of power* is also complained of by the patient. He notices it first in the arms, then in the legs, and finally in those muscles supplied by the bulb.

*Speech fatigue*, consisting in stiffness of the tongue, difficulty in expression and fatigue in talking, come late in the disease. They precede and generally inaugurate the symptoms of bulbar paralysis.

*Difficulty in swallowing* is a late manifestation. It accompanies the bulbar paralysis.

**PHYSICAL EXAMINATION.**—The physical findings determined by *observation* are those of atrophy, rigidity and paralysis. *Special tests* reveal exaggeration of all the tendon reflexes and fibrillary twitchings of the atrophied muscles. Efforts to talk and swallow precipitate the typical bulbar symptoms.

**LABORATORY FINDINGS.**—The laboratory findings are negative. There may be a mild degree of anemia, resulting from the enforced confinement and paralysis. Special examinations, with the exception of the electrical examination, add nothing. This, in the case of the atrophied muscles, is one of delayed or absent response to either faradism or galvanism or complete reaction of degeneration.

**Diagnosis.**—The diagnosis is made from the slow and gradual progress of an ascending atrophy and rigidity in a young adult and from the physical findings of atrophy, rigidity, spastic paraplegia, exaggerated reflexes and bulbar paralysis.

**DIFFERENTIAL DIAGNOSIS.**—The diagnosis lies between chronic anterior poliomyelitis, combined and lateral sclerosis, tumor of the cord, syringomyelia and progressive muscular atrophy.

It is distinguished from *chronic anterior poliomyelitis* by the additional symptoms of spastic paraplegia, and later by those of involvement of the bulb. It is distinguished from *combined and lateral sclerosis* by the additional symptoms of chronic anterior poliomyelitis and, later, by those of involvement of the bulb. It is distinguished from *syringomyelia* by the absence of sensory symptoms—especially the one of dissociation—the spinal curvature and the sympathetic paralysis. It is distinguished from *progressive muscular atrophy* by the additional symptoms of spastic paralysis, later by those of bulbar involvement, and by the peculiar distribution of the atrophy.

In making the diagnosis, the following essential points may serve as a guide:

*In favor of amyotrophic lateral sclerosis:*

1. Spastic paraplegia.
2. Symptoms of bulbar paralysis.
3. Rapid course—1 to 4 years.
4. Exaggerated reflexes.
5. Paralysis of the muscles before they atrophy.

*In favor of progressive muscular atrophy:*

1. No involvement of legs, no spasticity.
2. No bulbar paralysis.
3. Long course—15 to 20 years.
4. No exaggeration of reflexes.
5. Atrophy of muscles before paralysis.
6. Fibrillary twitchings.

*In favor of acute anterior poliomyelitis:*

1. Paralysis sudden before the wasting.
2. Rapid course.
3. All the muscles of one section of the limb are affected.
4. Location—most commonly, legs.

*In favor of syringomyelia:*

1. Peculiar sensory symptoms of this disease.
2. Deformity of spine.

*In favor of lead paralysis:*

In this condition the blue line on the gums, the history, lead colic, and drop wrist would settle the diagnosis.

**Complications.**—There are no complications, the disease being rarely seen otherwise than alone. Its duration is from two to eight years, and death results either from an intercurrent condition or from paralysis of the respiratory muscles.

**Clinical Types.**—The clinical types of the disease are three in number: (1) those cases in which the atrophy of the arms predominates; (2) those cases in which the rigidity of the legs predominates, and (3) those cases in which the bulbar symptoms predominate.

**Treatment.**—The treatment of amyotrophic lateral sclerosis is general, tonic and symptomatic.

**GENERAL MANAGEMENT.**—The general management is all important. **Regularity of life** should be insisted upon. A régime indicating the hours for rest, meals and baths will insure better care and afford help and encouragement. **Plenty of fresh air** is essential. The windows should be kept open at night; the patient should be encouraged to stay out of doors. Over-exertion and strain must be avoided. **Long periods of rest in bed** help. These patients require long nights, also a rest in the middle of the day. **Warm baths** improve the body nutrition and reduce the rigidity. **Massage** helps the progressing atrophy and affords slight exercise. The formation of contractures is most annoying and trying. These cannot be avoided, but **passive motions** may delay their progress. The interposition of **pads and cushions** will lessen the resulting pressure-pains and save erosions of the skin. The care of the latter is all important. In this disease there is no excuse for the formation of bed-sores. The **stomach-tube** should be used early, to accustom the patient to its use, as swallowing will later become difficult. The

**constant current** may be applied to the throat, with one electrode in front and the other at the back. This will induce artificially the swallowing movements.

The **care of the mental attitude** of these patients is almost as important as the physical. Unless they are taught to be cheerful and are educated to a proper viewpoint they will not do well. Occupations should be provided, interests suggested and encouraged. The early atrophy of the hands will prevent the usual occupations so that resort must be had to the intellectual. Reading and study must be insisted upon as part of the régime.

**Diet.**—The diet should be strengthening and fattening, while at the same time not constipating. Beef-juice will keep the hemoglobin and red-cells practically normal; butter, cheese, oils and bacon will supply the fats; fruit juices will supply the laxatives.

**MEDICINAL TREATMENT.**—The medicinal indications are limited to tonics, laxatives and, from time to time, mild sedatives. **Strychnin should be avoided** as it increases the rigidity and is too stimulating. **The constant use of laxatives is bad.** **Sedatives should be used with caution** to avoid the contraction of a habit and to prevent the development of a toxemia. There are occasions, however, when 5 grains of veronal (0.324 gram) will insure a good night and when 10 grains of sodium bromid (0.65 gram) will change a depressed or restless day into one that is bearable. As a general rule, drugs should be avoided. There is **no reason to use opium in any form** in this disease.

**Pathology.**—The essential character of the pathological process in amyotrophic lateral sclerosis is one of degeneration. The nerve-cells disappear, the meshwork of fibers is diminished and thinned. This process involves essentially the motor system, the sensory being spared. The involvement affects the entire motor system, so that the distribution is from the cortex to the periphery. The motor nuclei of the bulb, the cells of the corpus callosum, those of the pons and medulla, the direct pyramidal tracts, the cells of the anterior horns, and the spinal motor neurons are affected. This process of degeneration is centrifugal and progressive; it involves the whole motor system and is therefore a disease of the entire corticomuscular tract. Some authorities have found an atrophy of the pyramidal cells in the paracentral lobes, others have reported degenerations as occurring in the lateral columns, Clark's columns, the spinocerebellar tracts, and the anterior horns. It is, therefore, a disease which affects both upper and lower motor neurons.

**Historical Summary.**—The history of amyotrophic lateral sclerosis dates from about 1870. Previous to that time it was lost among the progressive muscular atrophies, where it might still have been, had not Charcot rescued it by describing a new disease of the spinal cord. He cited cases which combined the atrophy of anterior poliomyelitis with the spasticity of lateral sclerosis. His pupils added to its literature. About ten years later, in 1883, Déjerine showed that certain cases of bulbar palsy were really terminal cases of this new disease of Charcot. About this time it began to be universally recognized as a disease entity.

Marie, Holmes, Spiller, Raymond and others have contributed much to its clinical and pathological study.

### SPINAL MENINGITIS

The spinal cord is covered by two membranes called meninges—the dura mater and the pia mater. An inflammatory condition of either is called meningitis. The dura is external and thick, and consists of two layers; the pia is internal and soft. These two meninges are closely adherent, so that an involvement of the inner surface of the dura is very likely to extend to the pia, or the inner membrane. Therefore, the symptoms merge, rendering differentiation difficult.

The simplest way to understand the affections of the dura mater is to divide them into two types, according to which surface is involved: the external and the internal. The Greek word for thick is *παχύς*. Therefore, these two types of meningitis may be most appropriately called (1) external pachymeningitis, and (2) internal pachymeningitis.

The inner membrane, the pia mater, may also be affected in two ways, according to whether the condition is acute or chronic, and may be divided into (1) acute leptomeningitis and (2) chronic leptomeningitis.

#### AFFECTIONS OF THE DURA MATER

##### *External Pachymeningitis*

External pachymeningitis is an inflammation of the outer layer of the dura mater, the one which adjoins but does not touch the bony surfaces of the spinal column. It is a common disease and one which is secondary.

**Etiology.**—Pachymeningitis externa is due to the extension of diseased conditions. It is, therefore, secondary; the most frequent primary causes are tubercular abscesses, vertebral caries, bed-sores, and collections of pus in the immediate neighborhood.

**Symptomatology.**—**CLINICAL HISTORY.**—It first produces symptoms of irritation of both motor and sensory nerve roots. If it progresses, there are additional symptoms resulting from pressure upon the cord, the exact nature of which depends upon the affected region. The clinical story is one of pain, tenderness and irritation—the course chronic. The principal symptoms are pain in the back, radiating down the legs or arms, stiffness, muscular spasms, motor paralysis—late in the disease, hyperesthesia, sphincter disturbances, local tenderness and changes in reflexes.

**PHYSICAL EXAMINATION.**—The physical findings are few. There may be none except such as result from compression of the spinal cord.

**LABORATORY FINDINGS.**—The laboratory findings are negative unless they show signs of the primary condition.

**Diagnosis.**—Diagnosis is not difficult, provided the primary condition is recognized.

**Complications.**—There are few complications. External pachymeningitis is in itself a complication of tubercular conditions, vertebral caries, new growths, abscesses, tumors and purulent conditions.

**Treatment.**—The treatment is largely surgical. Orthopedic measures, such as braces and plaster jackets, help.

**Prognosis.**—The prognosis is bad except in those cases secondary to pressure. Relief of this, by orthopedic or surgical measures, is indicated.

**Pathology.**—The dura mater may be affected in one of three ways: (1) If the condition is mild, there will be a slight opacity and congestion of the dura mater, which may be circumscribed or general; (2) if the condition is purulent, there will be a complete covering of the membrane by a caseous or purulent substance; (3) if the condition is chronic, there will be fibrous tissue and nodes of thickening scattered over the dura mater. Either the pus or the hypertrophic tissue may be so extensive as to cause symptoms of spinal pressure.

### *Internal Pachymeningitis*

Internal pachymeningitis is rare. It is spoken of as "hematoma of the dura." Some authors subdivide it into two types—the hypertrophic and the hemorrhagic. The condition is a combination of hemorrhage and hypertrophy and can best be studied without subdivisions.

**Etiology.**—Syphilis and alcohol cause many cases. The condition, therefore, occurs most frequently in general paresis and chronic alcoholism. In extrameningeal hemorrhage, the most common cause is trauma. Other less frequent causes are the rupture of aneurysms, operative procedures, hemorrhages and certain diseases which induce spinal congestion. Infectious and circulatory diseases may cause slight hemorrhages. An internal pachymeningitis in the cervical region, due to syphilis, is occasionally found—hypertrophic cervical pachymeningitis.

**Symptomatology.**—**CLINICAL HISTORY.**—The onset is gradual and slow. The classic symptoms of meningeal irritation first appear, and later those of cord compression. The course of the disease is long, the advance gradual. The termination in the majority of cases is death, through exhaustion. A small minority remain chronic; a very few recover.

The symptoms are: pain, hyperesthesia, loss of power, atrophy, anesthesia, changes in reflexes, rigidity and paraplegia.

*Pain* is a constant and early symptom. It is violent, sudden, and resembles the pain in lumbago. It occurs over the site of the hemorrhage, and may, as a result of pressure, extend down the back and legs. It is not so evident on pressure as upon active motion. It is usually the first symptom and is often severe. It may be so localized as to enable the patient to indicate the exact point of tenderness. Pressure causes shooting pains in the legs and along the trunk.

*The hyperesthesia* involves both skin and muscles. It is general and extreme and conforms to the level of the lesion.

*The change in the reflexes* is to one of exaggeration.



**Pathology.**—The inner surface of the dura mater is covered with a dark brown exudate which may be circumscribed or diffuse. It is thick and matted, the result of successive hemorrhages. These hemorrhages occur in layers which tend to degenerate. The blood-clots, therefore, assume various colors, the older ones being yellow—the color of deteriorating blood—while the newer ones are bright red. Eventually there occurs a mass which causes pressure symptoms.

## AFFECTIONS OF THE PIA MATER

### *Acute Spinal Leptomeningitis*

**Etiology.**—Acute spinal leptomeningitis is a disease of infectious origin. Many instances have been reported in which cases have been ascribed to cold, trauma and exposure. It is now recognized that these are not sufficient causes. In practically every instance bacteria will be discovered to prove the infectious nature of the process. The proper explanation of those cases in which trauma is the apparent cause is that the injury has served as a port of entry for the microorganism.

The most common *predisposing cause* of acute leptospinal meningitis is infection. Abscesses of the ear, infected glands, carbuncles, septi-cemia, pneumonia (resulting in a pneumococcus meningitis), and influenza, are causative diseases. Cold, exposure, and season have no bearing on this condition, but overcrowding, such as occurred in army camps, facilitates the carrying of the meningococcus. The symptoms result from the presence of pus-producing organisms in the spinal membrane. Inasmuch as the membranes are thin and of low resistance the spread of the disease is rapid.

**Symptomatology.**—CLINICAL HISTORY.—*Mode of Onset—Symptoms during Progress of Disease.*—Acute spinal leptomeningitis is rapid and sudden in onset. There may be a few days of malaise, but usually the condition begins with a chill, or, in children, with a convulsion, followed by a rapid rise of temperature. These initial symptoms are followed by pain in the back and legs, rigidity, and tenderness over the spine. The stiffness begins in the neck but very soon involves the entire body. The head and abdomen are retracted, and in severe cases the legs are drawn up. The heart action, at first slow, becomes rapid and feeble. The temperature remains high and the rigidity increases. Kernig's sign and that of Brudzinski appear. The reflexes are all exaggerated. Babinski's sign is present. There is hyperesthesia of the skin.

The patient may remain in this condition for several days or even weeks. A state of semistupor develops. It gradually deepens into a profound coma and the patient dies. In those few cases in which recovery takes place, the temperature subsides gradually, the pulse becomes slow, and the patient, after several weeks, convalesces. The rigidity persists longer than any other symptom and may remain for several weeks. A few cases may recover incompletely, leaving the patient in a semi-helpless state or afflicted with minor paralyses.

*Objective Symptoms.*—The objective symptoms are: temperature, changes in the pulse, changes in the reflexes, changes in the eye-grounds, rigidity, paralysis, spasms, opisthotonos, vasomotor changes—*tache cérébrale*, symptoms of cord compression, Kernig's sign, Brudzinski's sign, nystagmus and skin rash.

The temperature rises at once and remains high throughout the course of the disease. In a few instances it may be subnormal.

The pulse is at first slow and strong, but as the condition advances becomes rapid and feeble. There is no distinct ratio between pulse and temperature. This lack of uniformity is sufficiently frequent to warrant emphasis as a diagnostic guide.

The reflexes are usually exaggerated, but may be absent.

The changes in the eye-grounds vary from a mild optic neuritis to a complete choked disk. If the condition continues for any length of time, optic nerve atrophy results.

Rigidity develops early in the disease. It first appears in the neck and gradually extends over the entire body. The head becomes fixed and retracted.

The paralyses may be transient or permanent. They are apt to involve the legs, bladder, or eye muscles.

Spasms of isolated muscles, of extremities, or of the entire body are frequent. They occur at the end of the second or third day.

Opisthotonos is a late symptom. When the disease is far advanced and the infection severe, the patient becomes rigid. There are a retraction of the head and a stiffening of the legs, so that the body assumes the shape of a bow, and the patient rests on the head and heels.

Vasomotor disturbances are evidenced by the condition of the skin. Upon the abdomen appears the typical *tache cérébrale*, that is to say a line drawn by the finger-nail on the skin leaves an intense red blush.

The symptoms of cord compression may occur late in the disease.

Kernig's sign is important and diagnostic. It consists of an inability to extend the leg, when the hip joint is flexed to a right angle. It appears early, accompanying the rigidity.

Brudzinski's sign occurs at about the same time as Kernig's. It consists of a drawing up of both legs when the head is flexed upon the chest.

Nystagmus, lateral in character, is frequent in the severe cases.

*Subjective Symptoms.*—The subjective symptoms are chills or convulsions, nausea and vomiting, pain, tenderness, hyperesthesia and headache.

The disease, like all septic processes, is ushered in by a chill, which is accompanied by a rise of temperature. The chill is severe and general. In children, a convulsion takes the place of the chill.

Nausea and vomiting are premonitory symptoms of this condition.

Pain is early, frequent, and severe. It may be localized or general.

There is always marked sensitiveness to touch. The eyes are peculiarly liable to photophobia. The spine and neck are unduly sensitive. There may be general hyperesthesia.

*Headache* is one of the most distressing symptoms. It is severe, and either frontal or general in location.

**PHYSICAL EXAMINATION.**—The physical findings are those of rigidity, exaggerated reflexes, Kernig's sign, Brudzinski's sign, tache cérébrale, retracted abdomen, optic neuritis, choked disk, sometimes nystagmus, and rapid and feeble pulse.

**LABORATORY FINDINGS.**—The laboratory findings in acute meningitis are of the utmost importance. *The blood*, while it does not reveal much, shows an increase in the number of red cells, but no marked increase in white cells. In favorable cases there is an increase of lymphocytes. There may also be an increase in the polymorphonuclears.

The most important information is given by the *cerebrospinal fluid*. The method of obtaining the latter is by lumbar puncture. It is a simple and harmless procedure and should be resorted to in every suspected case of meningitis. The changes which meningitis produces in the fluid are the following: (1) an increase in pressure; (2) changes in consistency; (3) changes in the number of cells, and (4) the presence of bacteria.

The *pressure* is always increased. So uniform is this that the severity of the disease may be measured by the amount of increase in the pressure. In severe cases this may be double the normal. The *consistency* of the normal fluid is clear and limpid. As soon as the meninges become involved, the change is to a slight cloudiness; as the condition advances, there is marked turbidity. The cells are increased. The more acute the process, the greater the number of cells. The *differential count* will reveal an increase in the polynuclear cells up to as high as 75 to 90 per cent., and large numbers of endothelial cells.

The most important information of all is the presence of *microorganisms*. There may be one of several types, or the infection may be mixed, the fluid containing two or three different types of bacteria. The most usual ones found are the pneumococcus of Friedlander, the meningococcus, and the streptococcus. It is sometimes exceedingly difficult to find any organism, so that in suspected cases a single examination of the cerebrospinal fluid ought not to suffice, nor should the pathologists give up hope of finding microorganisms until the search through the microscope has been long and faithful. The value of examining the cerebrospinal fluid in these cases lies in the fact that in only one of these types of infection has any serum been found to help the condition, that is, in the meningococcus type. If the infection should be caused by any of the other forms of microorganisms, the outlook is hopeless. If the type of meningitis is that caused by the meningococcus, the intraspinal administration of Flexner's serum will give immediate and good results.

A *blood-culture* made early in the disease will, in a great many cases of meningococcus meningitis, give positive results.

**SPECIAL EXAMINATIONS.**—Special examinations are of no avail in meningitic cases, and neither functional tests nor instrumental examinations throw light on the condition. X-rays are of no value.

**Diagnosis.**—The diagnosis is made on the clinical history, the physical examination and the laboratory findings.

**Treatment.**—The treatment may be classified under two headings: general and specific.

**GENERAL TREATMENT.**—The general treatment should be that of any acute illness. The patient should be put to bed and kept absolutely quiet. Owing to the rigidity and peculiar positions assumed, a **water-bed** will give the most relief and the best results. **Hot baths**, together with **hot and cold packs**, will relieve the rigidity and extreme nervousness. An **ice-bag** should be kept on the spine and at the base of the neck. The **skin must be kept clean and rubbed daily with alcohol** to prevent bed-sores.

**Diet.**—The diet should be liquid, and while the temperature is high, restricted to milk.

**SPECIFIC THERAPY.**—The specific treatment should consist of **lumbar puncture** and the use of **serum**. Frequent withdrawals of spinal fluid for the purpose of reducing intracranial pressure will relieve the rigidity and headache and lower the temperature. *In the septic types*, that is, the pneumococcus, streptococcus, etc., though the prognosis is practically fatal, **irrigation of the spinal canal with saline** has been known to have cured at least one case.

In one type, namely the meningococcus, a serum has been made which serves to destroy the microörganism causing the disease. The hope for cure lies only with this type. The only ill effects from the use of this serum—the danger of anaphylaxis—can be eliminated by the preliminary subcutaneous injection of 1 c.c. preparatory to an intravenous or intraspinal injection. There is, therefore, no contra-indication to administering this serum in any type of meningitis while awaiting the laboratory reports.

The more recent conception of meningococcus meningitis as a blood infection with localization in the meninges has resulted in a more complicated but also more successful method of treatment. Herrick has proven that the **combined administration of meningococcus serum, intravenously, with intraspinal injections** will give the best results, especially in the septic types. This treatment must be pursued unremittingly, especially in the early stages.

**MEDICINAL TREATMENT.**—There is no specific drug for acute meningitis, but small doses of **bromid** and **chloral** will quiet the patient and relieve the extreme nervousness. **Morphin** will be necessary for the headache. As the condition subsides **counterirritants** of a mild type may be applied to the spinal column, among which are **hot douches**, **mustard leaves**, and **light cauterization**. The **contractures and paralyses** will demand special care and should be treated from an **orthopedic point of view**.

**CONVALESCENCE.**—The convalescence is slow and much longer than the actual disease. The treatment in this stage is important. *For the paralyses* the patient should have **massage and electricity**. The elec-

tricity should be faradic, given gently and for a few minutes daily. **Braces and mechanical appliances** will help the *contractures*. The convalescence can be hastened by **attention to the general health**. A change of environment, country air in the summer, and good food, together with tonics and beef juice will help.

**Pathology.**—There are several pathological changes in spinal meningitis. There is first hyperemia, then exudation. This latter is, first, serous and then rapidly becomes fibrinous and suppurative. The meninges are covered with a sticky, gelatinous substance, and the spinal fluid is turbid. The distribution is diffuse, the posterior part being affected more than the anterior. In the tuberculous type pus is rarely present.

For some days the spinal cord escapes any involvement, owing to the resistance of the pia mater which covers it. If, however, the disease progresses for a sufficiently long period, the outer portions of the spinal cord show evidences of the invasion in the changes, congestion and hemorrhages occurring in the fine nerve terminals, in the tissues, and in the blood-vessels. Should the disease progress for some time the substance of the cord itself will become involved, softening will result, and the condition terminate in a myelitis. In meningococcus infection the recent advances made by Herrick at Camp Jackson and by Netler have shown that a small percentage of these cases never develop meningitis. The disease is essentially a bacteriemia which sooner or later localizes in the meninges. Its extrameningeal forms are characterized by purpura, polyarthritis, pleurisy, pneumonia, pericarditis, endocarditis, orchitis and involvement of the accessory sinuses. This viewpoint changes and simplifies our previous conception of the disease.

**Prognosis.**—The prognosis in meningitis is wholly dependent upon the type of microorganism found in the spinal fluid. In those cases in which the type of microorganism is virulent, and one for which no serum has been found, the prognosis is bad. In that type in which a serum has been found the prognosis is good.

### *Chronic Spinal Leptomeningitis*

Chronic spinal leptomeningitis is the name applied to a certain group of symptoms which are chronic, of long standing, and secondary to some other disease.

**Etiology.**—The cause is usually that of an acute leptomeningitis. It may be the result of tuberculosis, syphilis, alcohol, or trauma. It may be secondary to organic disease of the cord.

**Symptomatology.**—The symptoms are motor and sensory in character, pain and paresthesia being the most common. There may also be stiffness, paralysis and atrophy. The condition resembles the acute type but is not so severe.

**Treatment.**—The treatment is largely that of a chronic nervous disease. Hygiene, quiet surroundings, nutritious diet, tonics and iodid of potash give the best results.

**Prognosis.**—The prognosis, from the very nature of the condition, is bad.

**Pathology.**—The pathology is not well known. Adhesions between the meninges and degenerative conditions of the spinal nerves are almost the only definite pathological lesions.

## MULTIPLE SCLEROSIS

Multiple sclerosis is a disease of youth, characterized by numerous and variable symptoms. These arise from the presence of isolated or disseminated patches of sclerosis scattered over the entire nervous system.

**Etiology.**—The cause of multiple sclerosis is obscure. In fully fifty per cent. of the cases none can be ascertained. Many authors, Strümpell and Ziegler among them, regard it as a constitutional condition—one in which there is a tendency to proliferate the glial tissue. Oppenheim considers that the congenital anomalies of development merely lay the foundation of the constitutional condition which renders the individual more susceptible to those influences which are regarded as “causes.”

It is best, then, to assume predisposing conditions of poor nervous tissue, defective heredity, and bad personal reaction. The nervous system will probably show congenital defects; the nervous ancestry transmit an inferior strain. When such tissues come in contact with the acute infectious diseases, poisons, emotions, trauma and shock, at about the age of puberty—an age when nervous tissue is especially unstable—in many instances there results multiple sclerosis. This is all that can be said definitely in regard to the etiology. The fact that certain authors point out its occurrence following the infectious diseases does not necessarily prove that these are the causes; the disease would never have developed had not the soil been ripe. Cases of multiple sclerosis have been reported following the shock of an earthquake, tin-poisoning, and after an attack of scarlet fever. These authors, however, have failed to report the hereditary and congenital nervous tissue of the sufferer.

Climate, season and altitude have no effect on the occurrence of the disease. The condition is not more frequent in the city or country, among immigrants, in private families or in institutions.

It cannot be proven that it is an occupational disease, nor that workers in drugs, dust, fumes and acids are more liable to contract it than those otherwise employed. It is not a disorder of metabolism. Neither diet, worry, nor overexertion is a factor in bringing it about. Imperfect sewerage and contaminated water supply do not influence it. The fact that cases follow infections and pregnancy is, to the writer's mind, more proof that these conditions lower the vitality and resistance of the nervous system than that they are a direct cause.

**Symptomatology.**—**CLINICAL HISTORY.**—*Onset—Symptoms during Progress of Disease.*—The mode of onset is gradual, extending over months. The initial symptoms and the order of their appearance vary.

The condition advances slowly, varies markedly, and terminates in a typical and characteristic way. The first symptom may be weakness, dizziness, impairment of vision, or lameness. Then follow disturbances of vision or speech, a slight spastic paraplegia, or uncertainty in the use of the arms and legs. The reflexes of the lower extremities become exaggerated, the superficial epigastric reflexes disappear and the patient becomes ataxic. He may develop epileptiform or apoplectiform seizures. He may also have slight or severe paralyses of the ocular muscles, of the bladder, and of the extremities. The condition may tend to remit or may remain stationary for years. Three cardinal symptoms which are considered pathognomonic of the disease—nystagmus, intention tremor and scanning speech then appear. The patient finally presents the picture of one suffering from an extensive involvement of the cerebrospinal axis. In some cases the spinal symptoms predominate, in some the cerebral.

*Objective Symptoms.*—The objective symptoms are more marked than are the subjective. They are: motor weakness in legs and arms; spastic paraplegia in varying degrees with its accompaniment of rigidity, exaggerated reflexes, and more or less paralysis; tremor—which is characteristic, and known as “intention tremor,” nystagmus and other eye symptoms; affections of speech, apoplectic and epileptic attacks, mental symptoms, uncontrollable laughter, paralysis of ocular muscles, disappearance of the abdominal reflex, ataxia, and tremors of face and head.

*The motor disturbances* are of all symptoms the most frequent, the most characteristic, and the most numerous. They vary from slight disturbances in the use of the arms and legs to tremors, ataxias, and more or less complete palsies. A slight motor weakness or a sense of muscular fatigue is an early symptom. The patient may notice an uncertainty in walking, a slight stiffness, a tendency to stubbing of the toes or clumsiness in the use of the hands. The legs are less frequently attacked than the arms. Another early manifestation of motor weakness is shown in an impairment of the handwriting.

*The spastic paraplegia* is really an extension of the motor disturbances. It begins as such, advances, and towards the end becomes typical, assuming a scraping, shuffling and stiff gait.

*The tremor* appearing in multiple sclerosis is a prominent, constant and characteristic symptom. It is considered one of the three cardinal signs of the disease. It occurs in 75 per cent. of the cases. It is jerky, coarse and intentional, that is, it occurs when the patient attempts a voluntary act. It ceases in repose, and is exaggerated by excitement. The distribution of this tremor may be general towards the end of the disease. At the beginning it involves only the hands and arms; it may be unilateral, bilateral, or it may involve the head. It is not restricted to the muscles of the fingers or hands, but may even involve those of the shoulder. The character of this tremor is coarse and slow, the excursions are extensive, so much so as at times to interfere with the use of the arms. The handwriting always shows evidences of the tremor;

its jerkiness and irregularity may be one of the first warnings of the condition.

The symptom of *nystagmus* occurs in 50 per cent. of the cases. It is a movement of the eyeballs, rhythmic and regular in character, which is especially evident in the lateral direction but may occur in either the vertical or rotary axis.

*Eye symptoms, other than nystagmus*, occur in about one-half of the cases, and usually appear early. Oppenheim says that they often precede any other symptom. They consist of scotomas, slight optic neuritis, pallor of the optic disk, and partial optic atrophies. The distribution is irregular; one eye may be considerably affected while the other is immune. Occasionally choked disk has been reported. The color fields may show slight variations. These affections of vision are usually found by the examiner long before the patient observes any difficulty in seeing.

*Affections of speech* are noted in many cases, and almost always towards the end of the disease. Speech may be slow, halting, and jerky, or it may be scanning, which is particularly characteristic of this disease. This type is slow, with a tendency to divide the words, accompanied by long pauses. It is rhythmical, cadent, and an exact counterpart of the speech used in scanning Latin poetry.

*Apoplectic and epileptic attacks* occur. Seizures of this type occur in from one-third to one-fourth of the cases. They vary from giddiness and faintness to attacks of loss of consciousness and general convulsions.

*The mental symptoms* are neither constant nor prominent. There is weakness, which may progress to a dementia, mental confusion, involuntary laughing and crying, and lapses of memory. In other words, the mental symptoms are those of slight intellectual reduction.

*Uncontrollable laughter* is a symptom which is fairly frequent. Regardless of the patient's condition or environment, he cannot refrain from laughing in a loud and distressing manner.

*Paralyses of ocular muscles* occur. Ophthalmoplegia is rare and the reaction of the pupils usually normal. Paralyses involving the external muscles are not uncommon.

*Disappearance of the abdominal reflex* is an early, constant, and important symptom. It occurs in 75 per cent. of the cases. There are very few diseases in which this reflex is absent as early and as frequently as in multiple sclerosis.

Some of the other superficial reflexes may also be absent. Of these the most constant are the cremasteric and epigastric. These signs are of great value in making a diagnosis.

In advanced cases of multiple sclerosis *ataxia* is present. The arms are apt to be more affected than the legs. When the Romberg test is applied the patient suffering from multiple sclerosis will be more apt to sway anteroposteriorly while the tabetic will be more apt to sway laterally.

*Facial tremors* are rare but do occur in advanced cases.

*Subjective Symptoms.*—The subjective symptoms are: dizziness, hal-



*Hallucinations of smell and hearing.*

The sensory disturbances consist of slight anesthetic spots, and occasionally anesthesia to touch. Vision is often faulty, and the bone sensibility may

Bladder disturbances are frequent. Oppen occur in 80 per cent. of the cases. They simulate syphilis, and consist of leakage and inability

Headache is frequent and paroxysmal.

PHYSICAL FINDINGS.—The physical findings are those of beginning physical disability, and difficulty in walking. The age of the patient is important. Multiple sclerosis is a disease of youth and rarely occurs after thirty. Percussion and percussion yield nothing. Changes in the voice are unusual and unwarranted attacks of laughing and crying. Special tests in regard to the eye grounds and the reflexes are of value as they reveal scotoma and atrophy in the former and exaggeration in the latter. An absence of the abdominal reflex is frequent and important.

LABORATORY FINDINGS.—The laboratory findings are practically all in multiple sclerosis. There is nothing unusual, nothing abnormal to be seen by an examination of any of the exudates, transudates, secretions, or excretions. Neither the blood, urine, nor spinal fluid shows anything out of the ordinary. Nonne has recorded some positive Wassermann reactions in the spinal fluid but they are not of a sufficient number to warrant a conclusion.

Diagnosis.—The diagnosis of multiple sclerosis, except in the very early stages, is easy. It is a disease of youth. The diagnosis should be made on negative spinal fluid findings (except for the which in many cases shows a typical parietic curve), early onset, intention tremor, nystagmus and scanning speech. In these, the deep reflexes are exaggerated, while the epigastric are absent, the diagnosis is clear.

DIFFERENTIAL DIAGNOSIS.—In making the diagnosis, multiple sclerosis, ataxic paraplegia, general paresis, syphilis are the conditions which will suggest themselves to be confused with cerebrospinal syphilis, as both are multiple lesions. The pupil and the spinal fluid differentiate multiple sclerosis from all syphilitic conditions. Differentiating it from paralysis agitans the character of the age of the patient will help in the decision.

SPECIAL EXAMINATIONS.—Special examinations, tests, instrumental and x-ray examinations, are of no value.

Complications.—The complications are not numerous. The most apt to involve the eye and bladder. In the



stronger, less ataxic, and improve somewhat in speech and tremor. It is, therefore, wise to hold out hope of improvement. The duration of the disease is long, measured by years. The course of the disease is variable and tedious. Death usually results from exhaustion, infection, or from one of the respiratory complications. The prognosis as to restoration of function, provided the case is not too advanced, is somewhat hopeful.

**Pathology.**—The brain shows irregular atrophies, some internal hydrocephalus, and a thinning of the cortex. A cross-section reveals many irregular sclerotic patches. Throughout the brain, spinal cord, and the entire nervous system there appear patches of sclerotic tissue. The patches vary in size from that of a pin-head to 5 or 6 centimeters. Some patches are isolated, others are diffuse, and made up of a confluence of several little ones; some are completely sclerotic, others only partially. The distribution is diffuse, the character that of a hard cartilaginous substance, the color at first red, and later gray. These patches are made up of glia fibers. Within the plaques are small holes, around which the glia fibers terminate. These patches resemble little eyelets, situated in the midst of the nervous tissue. They have a special aptitude for locating in nervous tissue, and may affect both white and gray matter. They may, therefore, appear anywhere, in brain, cord, fourth ventricle, roots of the cranial or spinal nerves, or within the optic nerve itself. In some cases there occur hundreds of such patches, in other only scores. First there is a degeneration of the myeline sheath, then an increased growth of glia cells, followed by a formation of fat granule cells. This in turn is succeeded by the formation of glia fibrils. The axis-cylinders are uninjured. The whole process is progressive, and finally terminates in a complete hardening or sclerosis. The constant occurrence of remissions and relapses is strongly suggestive of the presence of a toxin.

**Historical Summary.**—The history of multiple sclerosis may be said to begin with the researches of Cruveilhier in 1835-1845, to which, later, Frerichs and Valentine contributed. The first real conception of the disease, however, was made by Charcot in 1862. He it was who considered the three leading symptoms—nystagmus, intention tremor and scanning speech—as manifestations of one disease.

### SUBACUTE CORD DEGENERATION

**Etiology.**—It is not possible to find any definite cause for this condition. It is not specific; it may result from a congenital defect. Risien Russell, Batten, and others think it may result from a toxin.

**Symptomatology.**—**CLINICAL HISTORY.**—Subacute cord degeneration is a condition which can best be understood by dividing it into stages, as the clinical course is gradual, the transition abrupt and marked. There are first sensory symptoms in the legs, then ataxia and rigidity, and finally complete paralysis and death—all occurring in the space of

a few months. Therefore, the disease may be divided into three stages: (1) the stage of pain, (2) the stage of ataxia, and (3) the stage of paralysis.

*In the stage of pain*, which ushers in the disease, the patient complains of tingling and slight pain in the legs and begins to notice that he has some difficulty in walking. This stage lasts for a few weeks and changes rather suddenly into the *stage of ataxia*. The difficulty of walking is much more pronounced and becomes both spastic and ataxic. The knee-jerks, contrary to what one would expect with ataxia, are exaggerated. As the condition advances, there is an abrupt change to the third stage. The spasticity gives way to *flaccidity and complete paralysis*, the knee-jerks disappear, Babinski's reflex remains, and the sensory symptoms of tingling and anesthesia become more extensive. Towards the end, the patient develops a temperature, loses control of both sphincters, and develops a mild degree of edema.

*Objective Symptoms.*—The objective symptoms are: ataxia, spasticity, paralysis, changes in reflexes, atrophy, edema and fever.

*Subjective Symptoms.*—The subjective symptoms are: numbness and tingling in the arms and legs, anesthesia, difficulty in walking, and loss of control of both sphincters.

**PHYSICAL EXAMINATION.**—The physical findings vary according to the stage of the disease. The patient at first is both ataxic and spastic, later paralytic and edematous. The examination of the reflexes in the beginning shows that they are exaggerated. As the disease advances the knee-jerks disappear, but the Babinski and superficial reflexes always remain unduly active.

**LABORATORY FINDINGS.**—The laboratory findings are negative.

**SPECIAL EXAMINATIONS.**—There is no special examination of any importance.

**Diagnosis.**—The diagnosis is made on the clinical history of a rapid onset, the combination of sensory symptoms and exaggerated reflexes, together with spasticity and ataxia. These symptoms, added to a negative spinal fluid, the appearance of edema, temperature, and later complete paralysis, in a young person, render the diagnosis easy.

**Complications and Sequelæ.**—The most common complications and sequelæ are infections resulting from the cystitis and bed-sores. There may also be accumulations of fluid in the joints and body cavities. The disease is not associated with any other condition. It may appear as one of two types—either the ataxic or the spastic. In some cases one predominates over the other, a condition dependent upon which columns of the cord are primarily involved. As the disease progresses, slight paralysis gives way to complete paralysis, and there develops a wholly different type—the paralytic.

**Treatment.**—There is no specific treatment for this condition. The only help which can be afforded is through **relief of the symptoms**. The symptoms are the usual ones occurring in spinal cord conditions. Their treatment has been fully described above under the heading *Myelitis* (page 297).

occur; in the joints painless swellings and pseudo-Charcot joints. These joint changes simulate those occurring in tabes, and, as in that disease, tend also to affect the larger joints in preference to the smaller. In contradiction to that disease, the larger joints of the upper extremity rather than the larger joints of the lower are affected. Trauma, while not the predisposing cause of such swellings, may often prove to be the exciting cause. These arthropathies are of two kinds—the atrophic and the hypertrophic. In the bones there occur brittleness, delayed union, tendency to fractures, and trophic changes simulating acromegaly.

*Deviations of the spinal column* are very common and occur in more than 50 per cent. of the cases. They may be either lateral or antero-posterior. The usual form, however, is scoliosis. The distribution may involve the whole spinal column or only a part. It usually affects the dorsal region because the site of the pathological lesion in this disease is most frequently dorsal. The cause given by most authorities for these deviations is atrophy of the muscles, causing an undue and uneven pull in one direction. Other writers believe that erosions and bony changes in the vertebral column are additional factors.

*Vasomotor disturbances* are common. The skin may be mottled, red, or swollen. There may be excessive perspiration.

*The pupillary symptoms* are important. *The Argyll Robertson pupil* does sometimes occur. More often there is simply *inequality with an enophthalmos and narrowing of the palpebral fissure of the corresponding eye*. These conditions arise from a paralysis of the cervical sympathetic nerve. *Nystagmus* is sometimes present. It occurs early and is the result of lack of muscular tone and coördination of the motor mechanism of the eye. The ophthalmoscope reveals nothing. Scotomata are not found. Rarely the visual fields are narrowed.

*Bulbar Symptoms*.—In those cases in which the gliosis involves the medulla oblongata the usual train of *bulbar symptoms*—paralysis of the tongue, lips, and pharynx—together with the difficulty in swallowing and the bulbar speech, follows.

*Spasticity, with the symptoms of spastic paraplegia* is common in aggravated cases and towards the end of the disease. It results from mechanical causes which interfere with the transmission of impulses from the brain, through the cord, to the periphery. Its character is stiffness with exaggerated reflexes, its distribution, usually the legs. The gait is spastic, that is, stiff and shuffling, so that the feet scrape along the floor and are raised with difficulty.

*The disturbances of reflexes* vary with the lesion. In those cases in which the involvement of the cord is most marked in the anterior horns, the reflexes are diminished or lost; in those in which the involvement is most marked in the lateral columns and pyramidal tracts, the reflexes are exaggerated. Therefore, the usual examination of the reflexes reveals diminished or absent elbow and wrist jerks, together with exaggerated knee and ankle jerks, Babinski reflex, Oppenheim reflex, and their modifications.

*Subjective Symptoms*.—The subjective symptoms are the following:

weakness and partial paralysis, difficulty in walking and stiffness, coldness, cyanosis, and injuries to the extremities, interference in speech, mastication, and swallowing, analgesia, tendency to burn and freeze the fingers and toes, bladder symptoms, and sensory disturbances—especially the symptoms of dissociation anesthesia.

*Weakness and partial paralysis* are early symptoms, first appearing in the hand and arm. They result from atrophy, and attack those muscles corresponding to the lesion in the anterior horn. The muscles of the back may become weak and the legs partially paralyzed as the result of an involvement of the pyramidal tracts and lateral columns.

*The difficulty in walking* follows the weakness of the arms. It begins by stubbing of the toes, then by dragging of the feet, and ends with *stiffness and paralysis* of both legs. The patient eventually presents a well-marked spastic gait. The knees are bent and turn in, the legs are stiff, and the feet drag.

*The extremities* are affected; the fingers and toes freeze. The patient states that one finger and thumb are constantly being frozen, or, if a smoker, that the same fingers are being burned. The condition is due to the loss of sensation to heat and cold, and to the loss of the sense of pain.

*Interference in speech, mastication, and swallowing* are not uncommon symptoms. They result from an involvement of the bulb and are late in appearance.

*Analgesia*—loss of the sense of pain—will not be complained of as much as boasted of by the patient, who usually discovers it only when called upon to hold something very hot or very cold.

Bladder symptoms occur when the lesion is low in the cord; they consist of retention, leakage and cystitis.

*The sensory disturbances* are by far the most important, the most frequent and the most characteristic of all the train of subjective symptoms. The loss of muscular sense, of touch sense, of pressure sense, and of localization sense is rare. Analgesia and thermo-anesthesia are almost invariably present. Charcot designated a particular symptom which he considered pathognomonic of the disease, and to which he gave the name of "the dissociation symptom." This consists of a combination of thermo-anesthesia and analgesia, together with the preservation of tactile sensation. The failure to recognize heat and cold occurs early; it is common and usually affects the arm and hand of one side. There is a sharp line of demarcation between the normal and abnormal. These patients, in other words, have the sense of touch preserved but fail to perceive pain, heat and cold. The loss of the sense of pain is common and usually follows the same area as the one involved by the thermo-anesthesia.

**PHYSICAL EXAMINATION.**—The physical findings, determined by *observation*, are those of a young person with a wasted hand and slightly raised or deformed shoulder. The patient may or may not walk with a

stiff and shuffling gait. He is emaciated. Close observation reveals the presence of whitlows, erosions, or fissures upon some of the fingers. The hand and fingers are wasted and claw-like; the whole extremity is cyanotic and cold.

**Special Tests.**—The superficial reflexes are not affected. The deep reflexes are exaggerated. There is a loss of sensation to heat and cold, together with a loss of the sense of pain, while at the same time the sense of touch is preserved. There may be a loss of the muscular sense, the pressure sense, and the sense of localization.

**LABORATORY FINDINGS.**—The laboratory findings in this disease are not important. The condition is not due to syphilis. The blood, urine, sputum, and the spinal fluid show nothing.

**SPECIAL EXAMINATIONS.**—Special examinations are of no avail in syringomyelia.

**Diagnosis.**—The diagnosis is made on three characteristic symptoms which are present in the large majority of the cases. One of the three, if present alone, should suggest the disease, two will render its presence probable, and three absolutely positive. The three symptoms are: (1) loss of the sensation of pain and of temperature, while in the same area the sense of touch is preserved; (2) progressive muscular atrophy, accompanied by paralysis; and (3) trophic disturbances. When to these symptoms, are added spastic paraplegia and deformity, with one shoulder higher than the other, the diagnosis is probable. Coupled with these physical findings is a clinical history of weakness, wasting, and paralysis of one arm followed by weakness, stiffness, and slowly advancing paralysis of one or both legs. Following the appearance of such symptoms the coldness and cyanosis of the hands, together with whitlows, cracks, fissures, and ulcerations, will confirm the diagnosis.

**Complications.**—Syringomyelia is a disease of long duration and may therefore have many complications. Any of the acute infectious or contagious diseases may attack the patient. Syphilis may be grafted upon syringomyelia, many psychoses may complicate it.

**Association with Other Diseases.**—It may be associated with tumors, amyotrophic lateral sclerosis, Friedreich's ataxia, acromegaly, Basedow's disease, general paresis, idiocy, pellagra, leprosy, or hysteria. The more usual course, however, is one that is uncomplicated.

**Clinical Varieties.**—There are many clinical varieties; they are probably more numerous than in any other nervous disorder. This fact can readily be appreciated when one considers the causes of this disease and the still more evident fact that the areas of destruction may involve any part or tract of the spinal cord. It is best, therefore, to arrange the types according to their anatomical distribution. The following varieties may occur:

(1) The anterior poliomyelitic type—that is, the one in which the predominant symptoms are those of atrophy due to an involvement of the anterior horns.

(2) The spastic type—in which the predominant symptoms are

those of stiffness and exaggerated reflexes, due to an involvement of the lateral columns.

(3) The posterior and median poliomyelitic type, in which sensory symptoms predominate—due to an involvement of the posterior and median columns.

(4) The Morvan type—one in which there is a predominance of peripheral symptoms. This type acquired its name from one Morvan who first described it.

(5) The lumbar type.

(6) The unilateral type.

(7) The bulbar type.

**DIFFERENTIAL DIAGNOSIS.**—Syringomyelia must be differentiated from progressive muscular atrophy, multiple sclerosis, amyotrophic lateral sclerosis, spinal hemorrhage, intramedullary tumors, and extramedullary tumors.

The differentiation from *progressive muscular atrophy* is a simple matter if the dissociation symptom, the spinal curvature and the spastic paraplegia are elicited. From *multiple sclerosis* the differential diagnosis is made by the presence of the dissociation symptom, the spinal curvature, the trophic disorders, and by the absence of nystagmus, scanning speech, the Romberg sign, and the intention tremor.

The differentiation from *amyotrophic lateral sclerosis* is comparatively simple. In the latter case there occurs a marked exaggeration of reflexes, a considerable degree of wasting which is not limited to any particular cord distribution, together with an absence of sensory and trophic changes.

The differentiation from *spinal hemorrhage* is more difficult as the symptoms are similar. A gradual onset points to syringomyelia, sudden onset, to spinal hemorrhage.

The differential diagnosis in the case of *intramedullary tumors* is very difficult, as the symptoms and history of both conditions may be alike. The differentiation in *extramedullary tumors* is also difficult.

**Treatment.**—The treatment of syringomyelia is general, tonic, and symptomatic.

**GENERAL MANAGEMENT.**—These patients are able to get about for a number of years and should be taught to pay especial attention to their general health. The physical resistance must be kept at a maximum. To accomplish this, **fresh air, nourishing food, and an avoidance of overwork and exertion**, are essential. **Warm gloves and stockings** are necessary, as the patient does not feel the cold and is therefore apt to freeze his extremities. Care must be exercised in smoking and in touching hot articles. The dissociation symptom prohibits recognition of heat and cold.

**Electricity and massage are of little help**, although the latter may be tried in the atrophic regions. The spinal curvature may cause pain and increase the paraplegia. **An orthopedic brace or plaster jacket** will often relieve these symptoms, reduce the deformity, and improve the



figure and personal appearance. The application of the **x-ray** has sometimes helped to diminish the stiffness. **Prolonged hot baths** also help this condition.

A cheerful mental condition—one which has adjusted itself to the fact that the condition is a chronic one—is always of immense help in combating the inroads of these progressive nervous disorders. Many of these sufferers from organic nervous diseases, by the adoption of a resigned but cheerful mental and moral attitude, can live a comparatively comfortable and happy life for many years. The status of the chronic invalid with his attendant, egotism, and so-called necessities, is one to be persistently avoided. In bringing about the proper mental and moral tone, and in creating a happy and suitable environment, the skillful and careful physician can be of immense help.

**MEDICINAL TREATMENT.**—Tonics from time to time are necessary. The best drugs include **iron, strychnia, arsenic, and cod-liver oil**. It is best to alternate these, having due regard for the constitutional needs. There is no specific drug for the disease. **Strychnia**, if given, should be in the form of the nitrate, 1/40 grain (0.00162 gram) daily. Care should be taken to avoid continuing this for any great length of time as it is cumulative in its effects and tends to overstimulate.

**Prognosis.**—The prognosis *as to recovery* is bad. No case of syringomyelia has ever been known to recover. It is manifestly impossible that a disease which is due to the formation of a cavity in the spinal cord could be other than chronic. Remissions do tend to occur. The length of the disease is measured by years. Patients have been known to live for forty years. The mode of death is usually from some intercurrent condition, as emaciation, bed-sores, infection, vesical disturbances, pneumonia, tuberculosis, or by the aggravation of the trophic disorders.

The prognosis *as to function* is not favorable. The paralysis and stiffness are due to destructive lesions, and therefore do not improve.

**Pathology.**—The pathology of syringomyelia begins with the formation of a glioma. This appears in the gray matter of the cord, extends, degenerates, and liquefies. There is, at first, foreign tissue and later a canal filled with fluid. This tumor, which is yellowish-brown in color and firm, is made up of spindle-shaped and oval cells, together with filaments around the blood-vessels, which in turn are surrounded by a sheath of neuroglia filaments. The next step in the life of this tumor is one of degeneration, which in syringomyelia assumes the form of liquefaction. It consists of fluid, fibrin, and broken down tumor cells. The liquid may be clear, viscid, or thick; it may resemble water or blood. The cavity may have no lining, a thin membrane, or none at all, or in one portion the membrane may be present while in another it is wholly absent.

The dimensions and positions of the cavity vary. It may be single or multiple, elongated or bifurcated; it may consist of one large cavity with several small offshoots. It may vary from one millimeter to the entire

thickness of the cord. The position is equally variable; its favorite localization is posteriorly in the gray matter; in extreme cases it involves the entire cord. It is unusual to find the anterior columns of the white matter affected.

The symptoms resulting from such a pathological process are variable, depending upon the particular spinal tracts involved. There are two ways in which these tracts are affected: one by actual destruction; the other by pressure from an adjacent soft bulging canal. If the pressure is extreme, there may be added symptoms resulting from inflammation, hemorrhage, and necrosis. Inasmuch as the location of this gliomatous tumor is usually posterior, the cardinal symptoms are sensory. If on the other hand the pyramidal tracts are involved, the gait is affected and the cardinal symptoms are motor. Again, if the anterior horns are involved, the cardinal symptoms are those of atrophy and muscular weakness, and finally, if the columns of Clark are involved the cardinal symptoms are trophic.

Upon autopsy, the general appearance of the spinal canal and meninges is normal. The cord is soft and fluctuating; it bulges at the point where the glioma originally appeared. The favorite site for this is the lower cervical and upper dorsal regions. When the dura mater is opened the full significance of the pathological process is evident. The contents of the cord are no longer solid—they vary from a semisolid mass to a complete liquefaction; in some cases they are clear, in others red and bloody. The cross section shows an ellipse or merely a slit, while the long axis may lie in any direction.

**Historical Summary.**—About 1834 Ollivier, of Angiers, applied the name syringomyelia to the condition which ever since has characterized this disease. It had been recognized years before this, and as far back as 1816 Rachetti, and in 1800 Portal, described cases illustrating this condition, relegating them to the medical curiosities. Little attention was given to the condition, and none to the pathology until about 1853. In that year Duchenne noted a case in which there was muscular atrophy. In 1860 various medical scholars began explanations of spinal cord cavities. Articles were written by Charcot, Joffroy, Kahler, Seyden, Schultze, and others. Simon, of Paris, added much to our knowledge. In the eighties, more interest was aroused in the condition. In 1888 Anna Baumler published reports of 112 cases. In 1897 Hinsdale, in this country, published a monograph on the disease reporting over 137 cases. In 1894 Schlesinger published a most complete and scholarly article on syringomyelia. To-day syringomyelia is universally recognized and accepted.

## MUSCULAR DYSTROPHIES

**Etiology.**—The disease begins in infancy and seems to be more common among boys than girls. Heredity is an important factor and in most instances there occurs a neuropathic condition in the ancestry. Neither syphilis nor alcohol is a factor, but occasionally injuries and acute diseases seem to inaugurate the condition.

**Symptomatology.**—The dystrophies are made up of several groups. There are *certain features common to all varieties*, which Savill has enumerated as follows:

- (1) The presence of an hereditary taint.
- (2) The familial tendency.
- (3) The fact that the disease dates from early life.
- (4) The slow course.
- (5) The presence of muscular wasting which, wherever it may begin, becomes widespread and finally involves all muscles.
- (6) The absence of any definite reaction of degeneration.
- (7) The absence of any sensory changes.

*These varieties differ from one another in the following respects:*

- (1) The particular age at which the symptoms first appear.
- (2) The particular group of muscles first involved.
- (3) The presence or absence of hypertrophy.

**CLINICAL HISTORY.**—*Mode of Onset—Symptoms during Progress of Disease.*—The disease begins gradually and insidiously. Weakness, clumsiness, and wasting of the muscles are the principal symptoms. The distribution varies; it may begin in the arms, legs, or trunk, and eventually becomes widespread. The facial muscles are only occasionally involved. A certain degree of hypertrophy accompanies the atrophy, varying according to the type.

These patients assume unusual and typical positions. In some the atrophy of the legs causes a frog-like attitude; in others the atrophy of the shoulder-blades gives a wing-like appearance; in others the atrophy of the trunk muscles causes an abnormally erect position with kyphosis; in still others the hypertrophy of the calf muscles gives the patient an unwarranted appearance of strength and wellbeing.

The condition advances to a semi-helpless state, rarely to one of complete paralysis. The duration of the disease is measured by years. The patients die from exhaustion, intercurrent conditions and respiratory disorders.

It is characteristic of the disease to assume various types. The symptoms, therefore, vary in distribution, number, and extent, different types presenting different clinical pictures.

**Objective Symptoms.**—The objective symptoms are: atrophy of certain muscles or groups of muscles, hypertrophy of certain muscles or groups of muscles, motor weakness, characteristic attitudes, gait disturbances, loss of reflexes, electrical changes, deformities.

*Atrophy* is a leading symptom. Its distribution varies according to the type of the disease. It may be limited to a particular region, or it may become widespread; it may progress slowly, or it may at any time become arrested. *Hypertrophy* also varies according to the type of

the disease. It is less general than the atrophy. Its distribution is most frequent in the calf muscles. *The motor weakness* is one of the earliest symptoms. *Characteristic attitudes* arise from the effort on the part of the patient to adjust himself to the weakened and wasted muscles. He may be unable to walk, rise, or make proper use of his arms.

A peculiar position assumed, and one which is pathognomonic of this disease is the attitude of the patient rising from the floor. The patient turns over upon all fours. He raises the body with his arms, and then slowly moves the hands along the floor until he reaches the legs. The hands are then slowly pushed up along the legs to the knees, and from the knees to the thighs, until finally he stands erect. He really climbs up his own body. This manner of rising from the floor is confined exclusively to this disease.

*The gait* is best described as waddling. It occurs in those types in which there is an atrophy of the leg muscles. The patient then has to call to his aid the muscles of the trunk and so gives the effect of walking from his hips. The gait is duck-like, and not unlike that of a pregnant woman. *The deep reflexes* gradually disappear. If there is much hypertrophy about the legs, the tendo achillis reflex is present and sometimes exaggerated. There is a loss of *electrical excitability*, but no definite reaction of degeneration. *Deformities* appear after the atrophy is well advanced. They assume many types—the winged scapulæ, the arm characteristic of the living skeleton, the enormous calf muscles, the hollow back, the protruding abdomen, and the tendon contractures.

*Subjective Symptoms.*—The subjective symptoms are: weakness and clumsiness.

*The weakness* is the first symptom to attract the patient's attention. Its distribution is in accordance with the distribution of the atrophy and most commonly, appears in the hands or legs. *Clumsiness* soon follows weakness and often calls the attention of the patient to the atrophy.

**PHYSICAL EXAMINATION.**—The physical findings are those of atrophy with hypertrophy, weakness, unusual attitudes, a waddling gait, and loss of reflexes occurring in a young person. It often affects several members of a family.

**LABORATORY FINDINGS.**—The laboratory findings show a marked decrease in the pre-formed creatinin in the *urine*, together with an unusual amount of creatin. In the *blood*, the creatin is normal in amount, but the creatinin is low in value. There is also a definite hypoglycemia together with a delayed glucose utilization and altered sugar tolerance. Nothing is found in any of the *transudates* or *exudates*.

**SPECIAL EXAMINATIONS.**—The *x-ray* has revealed several rather constant abnormalities in the skull. A large percentage of the cases show pineal shadows and also an alteration in contour or size of the sella turcica and the clinoid processes. Rarefaction of the skull and long bones is sometimes seen.

**Diagnosis.**—The diagnosis is not difficult. It is made on the presence of atrophy and hypertrophy occurring in a young person, together with loss of reflexes, deformities, and the peculiar method of rising from





that in some cases the pathological changes have been strictly limited to those occurring in the muscular system.

**Historical Summary.**—The history of the dystrophies dates back to the time of Duchenne. He first wrote of a pseudohypertrophic condition in 1849. Twenty years later he classified them as myoscleroses. In 1876 and 1879 Leyden and Möbius wrote about the hereditary characteristics. To Erb, however, is really due the greatest credit in clarifying the situation. In 1883 he called attention to the muscular origin of some cases as distinguished from the nervous origin of others. He described a particular type—that known as the juvenile—which has ever since borne his name. A year later Landouzy and Déjerine described another form, and still later Charcot, Marie and Tooth added another. In 1910, Batten wrote a classical article summarizing our knowledge up to that time. Gordon Holmes contributed to the knowledge of the condition, and more recently still Timme and Goodhart have called attention to the endocrine theory of the disease.

## CHAPTER III

### TUMORS OF THE SPINAL CORD

By ISRAEL STRAUSS, A.M., M.D.

Definition, p. 337—Etiology, p. 337—Symptomatology, p. 338—Extramedullary tumors, p. 338—Intramedullary tumors, p. 345—Localization, p. 346—Tumors in the cervical region of the cord, p. 346—Tumors of the thoracic cord, p. 356—Tumors of the lumbar and sacral cord, p. 357—Tumors of the conus medullaris, p. 360—Diagnosis, p. 362—Differential diagnosis, p. 362—Diagnosis on laboratory findings, p. 374—Treatment, p. 375—Course, duration and prognosis, p. 378—Pathology, p. 381—Extramedullary tumors, p. 381—Intramedullary tumors, p. 384—Bibliography, p. 394.

**Definition.**—The title, "Tumors of the Spinal Cord," as used in this chapter, includes all tumors which interfere with the functions of the spinal cord by compressing it from the outside, or by invading the cord, as well as those which originate within the spinal cord itself. The word "tumor," as used here, embraces granulomata, parasitic cysts, and neoplasms proper; also inflammatory cysts of the pia and arachnoid membranes. The general discussion of spinal gliosis or syringomyelia will be found in another chapter. The author will, however, attempt in the section on diagnosis of spinal cord tumors to point out the differences between the two conditions.

**Etiology.**—**PREDISPOSING CAUSES.**—*Trauma.*—Although a history of trauma, concussion, or a blow upon the spine is very frequently obtained from patients suffering from spinal cord tumors, as antedating the onset of symptoms, it seems that no definite relationship can be established between these as a causation of the disease. Some writers, while they do not attribute directly the new-growth to trauma, claim that the growth of an already existing tumor may be hastened by an injury to the spine. In the opinion of Mills, when a predisposition does exist, a fall is more apt to produce osteoma, carcinoma, or fibroma than any other tumor. Other writers believe that injuries are a factor in the metastasizing of tumors. It seems to the writer that none of these claims are based on sufficiently strong evidence to enable us to ascribe trauma as a causative factor in the production of spinal tumors, any more than of tumors in any other part of the body.

**Age.**—As far as age is concerned, it may be said that no age is free from liability and no age is peculiarly liable to spinal cord tumors. Of 100 cases collected by Starr (intravertebral tumors), 70 were in patients above 15 years of age, and 30 were in patients under 15. Of Frazier's 330 cases, 4 were in the first decade of life, 24 in the second, 61 in the third, 63 in the fourth, 84 in the fifth, 39 in the sixth, 17 in the seventh, and in 38 cases the age was not stated.



The following table represents the age incidence in 82 cases collected by Armour from the National Hospital, London:

Years	Vertebral Carcinoma	Vertebral Sarcoma	Spinal Tumors	Medul- lary	Intramedul- lary	Extra- medul- lary	Both
1st decade	0	0	1	1	0	0	0
2d "	0	4	10	2	3	4	1
3d "	0	1	11	3	5	3	0
4th "	1	3	12	4	5	3	0
5th "	6	1	17	2	10	4	1
6th "	2	2	5	1	4	0	0
7th "	3	1	1	0	1	0	0
8th "	1	0	0	0	0	0	0

Of 400 cases collected by Schlesinger, 126 were intramedullary and 239, extramedullary. The extramedullary included 151 intradural and 88 extradural growths.

In the experience of most clinicians, tumors are very rare in children with the exception of tuberculoma, which Schlesinger says is one of the most common of the intramedullary growths in children under the age of ten.

*Sex.*—As to sex, it is believed that spinal tumors have a greater tendency to develop in males; this, however, is not borne out by actual statistics. Although of Frazier's 330 cases there were 169 males and 135 females (26 cases in which sex is not stated), thus bearing out such contention, we are inclined to think that this is a mere coincidence, and that no such actual predominance of tendency to spinal cord tumors in the male exists.

**Symptomatology.**—In the consideration of the symptomatology of tumors of the spinal cord, it is well to discuss the extramedullary and intramedullary growths separately.

**EXTRAMEDULLARY TUMORS.**—Oppenheim divides the symptoms caused by these tumors into three phases: (1) the phase of root involvement; (2) the phase in which there is beginning compression of the spinal cord; (3) the phase in which the compression has increased to such an extent that it produces a clinical picture of transverse section of the spinal cord.

(1) *First Phase.*—The important symptom of this stage is the presence of *pain*. This pain is due to the involvement of one or more posterior roots of the cord. It may be preceded by symptoms of irritation such as paresthesia, hyperesthesia, and, if the pressure upon a root or roots is sufficiently severe to interfere with conductivity, hypesthesia and even complete anesthesia in the area supplied by the root or roots may supervene. Paresthesia may take the form of tingling, numbness, formication, itching, or burning. Pain in the beginning may be slight. It is limited to a definite area, and later on becomes more severe, paroxysmal, and neuralgic in character. The pain is burning, cutting, and shooting in character. It may precede the development of any other symptoms for a considerable period. Cases have been reported in which pain was the only recognizable symptom for two to six years. Very frequently the significance of the root pain is not appreciated by the physician, and is regarded as of psychic origin, the patient being treated accordingly.

Just as in the gastric crises of locomotor ataxia, this pain is sometimes mistaken for gall-stones or renal colic. The author has seen one case of spinal cord tumor in which first the appendix and later on the gall-bladder were removed, and not until a neurologist recognized the presence of an extramedullary tumor was the patient relieved. Pain, radiating down the upper extremity, has been mistaken for angina pectoris. Any case in which there is a complaint of a localized persisting neuralgic pain, with or without objective sensory symptoms, is to be regarded with suspicion, and considered as being possibly due to a spinal neoplasm, unless some other etiological factor can be definitely established. Occasionally the pain is of a "girdle" character and is accompanied by a "girdle" sensation, or constriction. The pain is not always constant; there are periods of remission. Changes in posture, especially extreme extension and flexion of the head, when the neoplasm is in the cervical and upper dorsal regions of cord, or sneezing and coughing, may intensify the pain. The distribution of the pain and the associated sensory disturbances are very frequently of great value in localizing the site of the neoplasm. A number of cases have been reported in which the symptom of pain is absent throughout the entire course (Bailey, Clark, Oppenheim, Schultze and Sibelius).

Serko, in summing up the cases reported in the German literature of the past fifteen years, found that about one-half of the extramedullary neoplasms did not present a neuralgic stage. Occasionally the pain from a tumor of the cervical and upper dorsal region may be present in the lumbar region or in one extremity.

Nonne reported a case in which, although the tumor involved the 7th and 8th cervical segments, exerting pressure on the cord from one side and upon the posterior column, giving rise in the beginning only to ataxia in the lower extremities, it for a long time caused pain in the lumbar region and in one leg.

Heilbronner, Oppenheim, Cushing, Thompson, Flatau and Zilberlast, Henscher, Lenander, and others have warned against laying too much stress upon the distribution of pain in diagnosing the localization of the growth. The presence, however, of sensory disturbances associated with or without pain, is an important localizing symptom. Very frequently, in fact, almost always, there is localized tenderness of the spinous process of the vertebræ. This tenderness is also of importance as a localizing symptom, because it indicates the proximity of the neoplasm in growths of the spinal column.

The pain of spinal cord tumors may appear in regions which do not correspond in any way to the root segments which the tumor compresses. Flatau describes an extramedullary tumor at the level of the 8th cervical and 1st dorsal segments in which the pain first appeared in the left foot. Rainson-Thompson observed a case of extramedullary sarcoma which extended from the 8th to 9th dorsal root, and the patient complained of pain not only in the epigastrium, but also in the lower dorsal vertebræ and in the legs. In one of Oppenheim's cases the tumor in the middorsal region caused pain principally in the legs. Abrahamson had a case where the tumor at the level of the 7th cervical segment gave as its first sensory symptom paresthesia in the legs. Occasionally the pain radiates upwards rather than downwards.

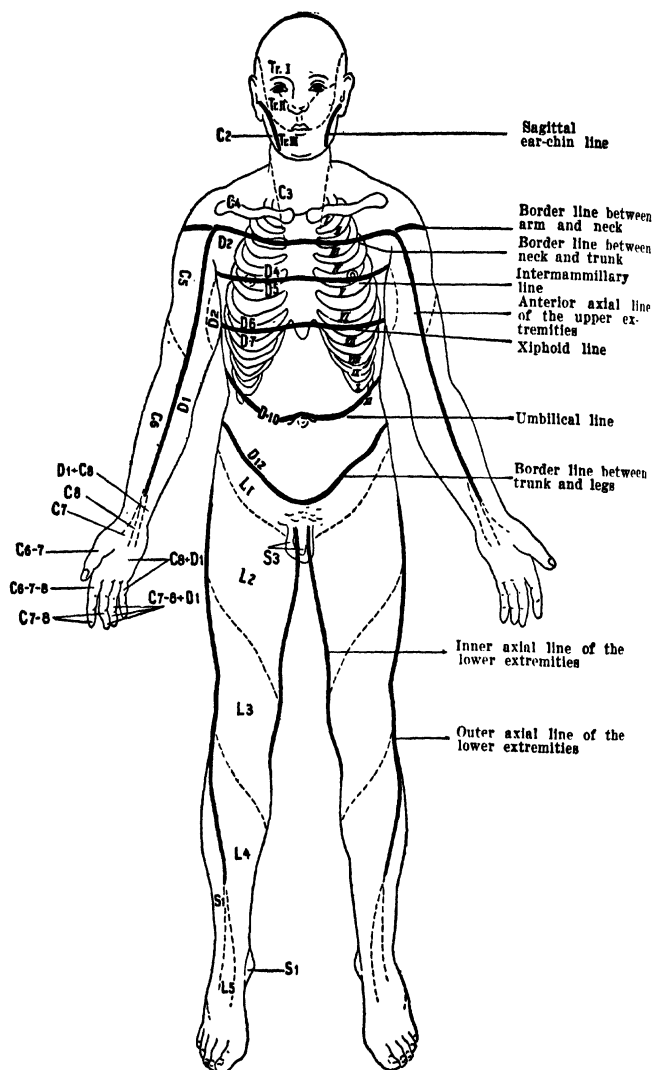


FIG. 1, A.—DIAGRAM OF SENSORY INNERVATION BY SEGMENTS, ANTERIOR. (After Flatau.)  
The heavy, continuous lines indicate the lines of direction or border lines, the broken lines indicate the dermatomes.

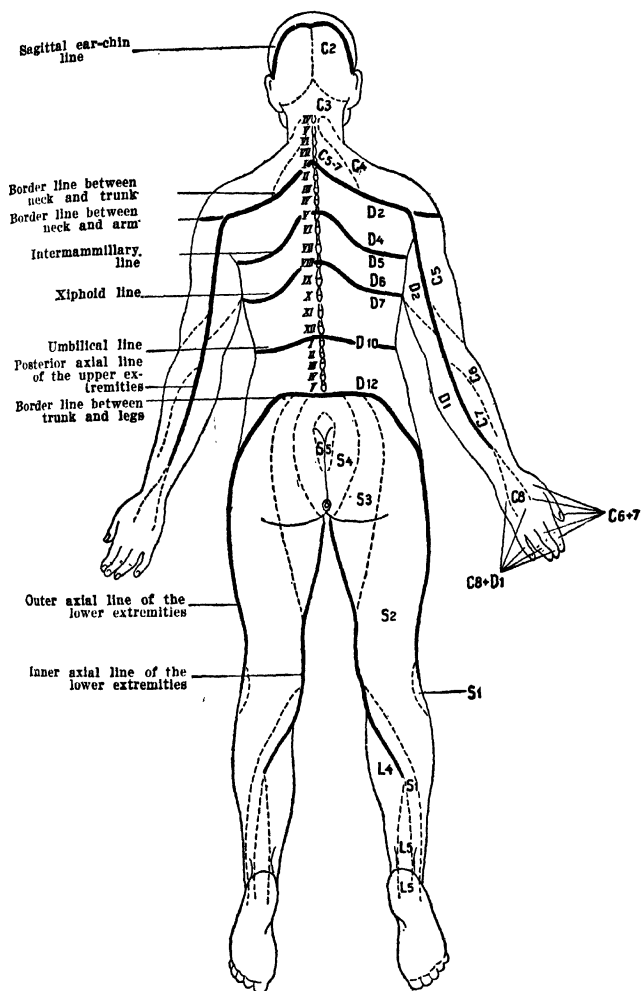


FIG. 1, B.—DIAGRAM OF SENSORY INNERVATION BY SEGMENTS, POSTERIOR. (After Flatau.)



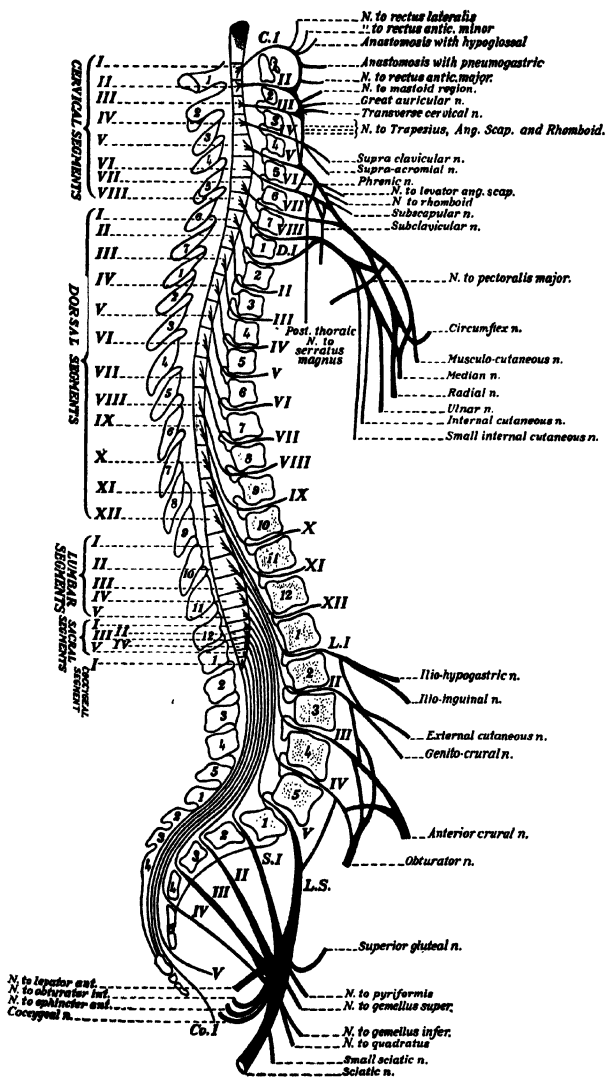


FIG. 2.—THE RELATION OF THE SEGMENTS OF THE SPINAL CORD AND THEIR NERVE-ROOTS TO THE BODIES AND SPINES OF THE VERTEBRÆ. (Déjerine and Thomas, from Frazier's "Surgery of the Spine and Spinal Cord," D. Appleton & Co.)

*Deformity* is very apt to appear early in the course of the disease, especially in malignant disease of the vertebral column; this is generally limited to two or three vertebræ. It is of far greater significance than postural scoliosis which may appear later in the course of an extramedullary, not necessarily bone, neoplasm.

*Paralyses* during the first phase may be met with, but they are very rare. This is because the neoplasms involving the anterior roots are not very common. Occasionally, especially in the cervical region, there may be an atrophy and paralysis of a few muscles of the upper extremity, due to anterior root involvement.

Pain in tumors of the lumbar cord may for a long time be limited to one side of the body. Tumors in the region of the sacral cord generally cause pain in the sacral region. In a few cases the pain is strictly localized.

The following case cited by Frazier,\* which was under the observation of Dr. Charles K. Mills, at the University of Pennsylvania Hospital, is one illustrating the irritative phenomenon of motor roots:

CASE I.—“The patient, a young woman, in February, 1912, began to have dull, aching pains in the back, in the region of the 4th and 5th thoracic vertebræ. Two months later, the lower limbs became weak and unsteady, and then completely paralyzed, paralysis of the bladder occurring at about the same time. The most distressing feature, however, was the intermittent spasmodic contractions of the legs, which were frequent, especially at night; at times they were severe enough to raise the legs to a considerable height, and at other times the jerkings were confined entirely to the feet. There was profuse sweating at night. Thermal and pain sensations were impaired up to the level of the 4th rib, and there was an increasing sense of constriction about the body at the highest level of impairment of sensation. At times, there was also disturbance of muscle sense in giving the impression that the lower extremities were raised when flat and vice versa.

“The lesion was thought to be in the spinal canal at the level of the 4th and 5th thoracic vertebræ.”

(2) *Second Phase*.—The characteristic symptom of this phase is the development of a Brown-Séquard syndrome—viz.: paralysis or paresis of the muscles on the same side and below the level of the lesion, with a loss or diminution of sensation of pain and temperature on the opposite side. The sense of touch may be markedly diminished on the paralyzed side, and may be diminished to a lesser degree on the opposite side. This syndrome is common in cases of extramedullary tumors, because most of these tumors exert their pressure on the anterolateral and posterolateral aspects of the cord. Disturbances of deep sensibility, such as the muscular and vibratory sense, as a rule develop very early in this stage. If the neoplasm lies on the posterior aspect of the cord and exerts its pressure first upon the posterior columns, deep sensibility is interfered with, and there may be a consequent ataxia in the extremities below the lesion. Occasionally the Brown-Séquard syndrome is absent, probably because the unilateral compression extends very rapidly to a compression of the entire cord.

\* Frazier, “Surgery of the Spine and Spinal Cord,” 1918, p. 529.

In the following case which came under the writer's notice, although there were symptoms of motor and sensory paraplegia when the patient first came under observation, a careful sensory examination revealed

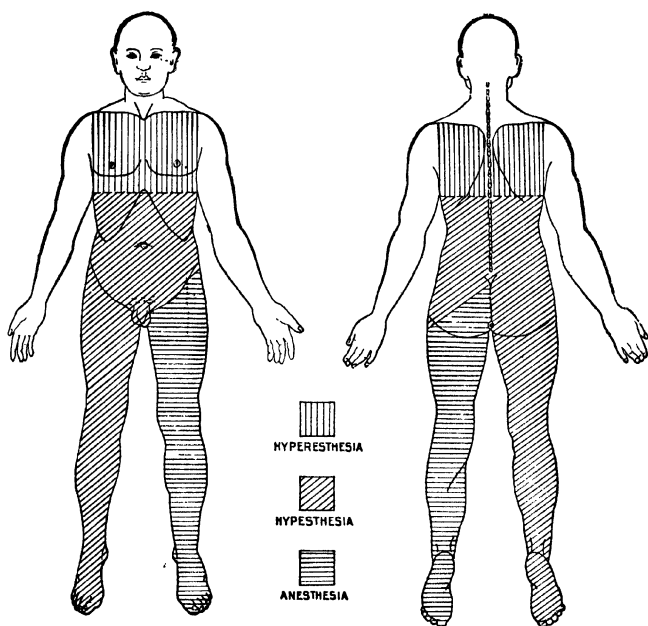


FIG. 3.—CHART OF SENSORY DISTURBANCES IN CASE II. (J. B.)

enough to indicate that there had been a Brown-Séquard syndrome, earlier in the course of the disease.

**CASE II.**—J. B., 63 years old, was admitted to Mt. Sinai Hospital on December 27, 1918, complaining of pains in the epigastrium and over the dorsal spine for the last five and one-half months, weakness of the lower extremities for the last four weeks, and paralysis of these for the last two weeks.

His previous and personal history are of no significance. His present illness began five and one-half months before admission, with pain in the pit of the stomach radiating to the upper back. The pain was so severe that he could not sleep at night. He had no nausea or vomiting. His physician ascribed his pain to some gastric disorder. Four weeks before admission, while at work he felt that his legs suddenly began to shake and



were beginning to give way under him. He could not stand without support. He was taken home and kept in bed chiefly on account of pain in his back and chest. With an effort he could still get around, but two

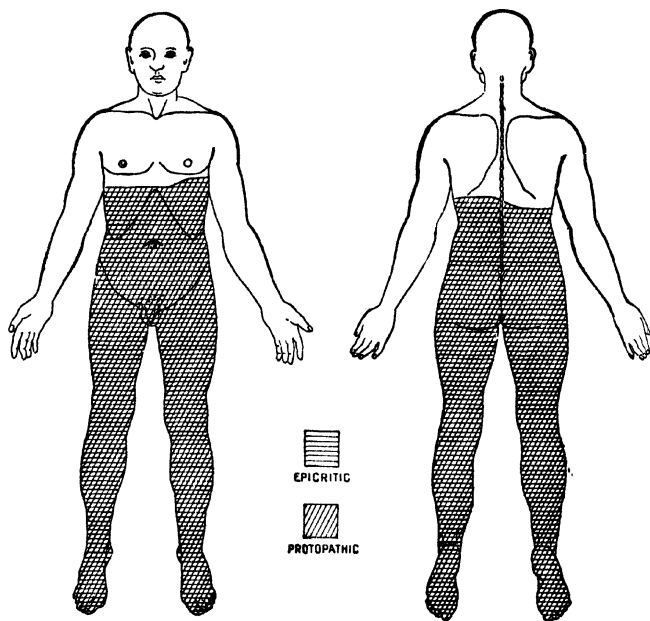


FIG. 4.—CHART OF EPICRITIC AND PROTOPATHIC SENSIBILITY IN CASE II. (J. B.)

weeks ago he suddenly fell down; after this he could not move his legs, although he *could* move the toes of the right foot for about one week. Two days after he fell, he noticed that he could not empty his bladder and a few hours later his urine began to flow involuntarily, and he had lost control of his anal sphincter.

Examination on admission revealed slight rigidity of the neck; tenderness over the dorsolumbar spine, more marked over the dorsal region, which was also somewhat angulated; the upper extremities were normal; all abdominal reflexes were absent; both lower extremities were weak, the left more so than the right, and somewhat spastic; both knee-jerks were diminished, in fact they could be elicited only upon reinforcement; Achilles-jerks, present but weak; no clonus and no Babinski; positive Kernig on left side. There were loss of pain and temperature sense below the 7th dorsal; loss of tactile sensibility and a zone of hyperesthesia, anteriorly and posteriorly between 1st dorsal and 7th dorsal, hypesthesia below

this on the right side, and anesthesia on the left. He also had retention of urine with overflow incontinence.

The sensory disturbances present at this time indicated that there had been at one time a Brown-Séquard type of sensory disturbance caused at the beginning by a lesion on the right half of the cord, although the paralysis was complete in both legs; the left side at this time still showed slight spasticity. The history of a complete paralysis of the left leg, with retention of power to move the toes of the right leg, was additional evidence of the lateral localization of the lesion. The appearance of root pains ("girdle" sensation), and the long duration of pain before the onset of the paralysis spoke for an extramedullary type of lesion. The rapid progress of the disease, the age of the patient, and the angulation of the spine, spoke in favor of malignancy. Tenderness over the 5th dorsal vertebra, with the zone of hyperesthesia in that vicinity, and with the other sensory changes below it, were the determining factors in deciding the upper level of the lesion. With these facts at hand it was decided to do a laminectomy, on the performance of which an extramedullary tumor was found in the bone, compressing the cord in the 5th thoracic region. Microscopic examination of the tumor proved it to be carcinoma.

Oppenheim has likewise reported a similar case. Serko has called attention to the fact that, in the restoration of a sensation after a decompression operation, the Brown-Séquard syndrome may appear, which he believes had been hidden by motor and sensory paralysis.

The *sensory disturbances*, which are due to cord compression in this stage, develop in an ascending fashion, and after removal of the compression, they are restored in a descending fashion. The first disturbance of sensibility usually appears in the legs, and involves the trunk at a later period. In typical cases, the sensory disturbance begins in the distal part of the leg, and ascends from there upwards—ascending upwards in front, and descending downwards behind. In some cases, the ascending sensory disturbances avoid the sacral segments. The development of these sensory disturbances is due to the position of the long sensory tracts in the cord, and the manner in which extramedullary growths exert their pressure upon these tracts. In this phase, the pressure upon the lateral columns of the cord may be so slight as to cause only a weakness in the muscles affected. This weakness may, however, rapidly change to a well-defined paresis. In some cases, pain as a premonitory symptom may be of very short duration; in others, paralysis develops very rapidly; and in still others, the patient may *suddenly* lose the power in his limbs. This sudden loss of power, however, does not last very long, but is soon replaced by a form of weakness, as described above, which is more marked in one-half of the body than in the other. Occasionally, the muscle weakness precedes the development of sensory disturbances. This is well illustrated by the following case which the writer had an opportunity to observe at Mt. Sinai Hospital:

CASE III.—A woman, 36 years old, had a fall which was followed one month later by a dragging of the right leg; one month after this, both legs became paretic, and eight months following this they had become totally paralyzed, and then for the first time the patient began to experience

paresthesiæ in both feet for a short period. Examination at this time showed no sensory disturbances whatsoever, complete paralysis of both lower limbs, with flexure contracture, and with very marked and painful reflex spasms. Subsequently, there appeared a small area to the right of the spine, between the 3d and 6th dorsal vertebræ, in which touch, pain and temperature sense were diminished. By this time there was also involuntary urination and defecation. The area of anesthesia was stationary for a period of one month. The diagnosis lay between spinal cord tumor, posttraumatic pachymeningitis, or callosities springing from fractured vertebræ, and lateral sclerosis; x-ray examination on two occasions was negative. Exploratory laminectomy was performed at the site indicated by the slight sensory disturbance. Unfortunately, the dura was not opened, the surgeon feeling certain that there was no tumor underneath the dura. The wound healed by primary union, but the patient was unimproved, and the condition increased, so that eventually symptoms of a complete compression of the cord appeared and the patient died. At the autopsy, a fibroma was found, situated laterally and dorsally on the cord, compressing the nerve-roots in the region of the 8th cervical and 1st dorsal vertebræ—within the dura, just above the site of the operation. The compression of the cord was considerable, and yet the sensory disturbances of root involvement were slight, and nothing like what would be expected from compression of the sensory tracts in the cord.

This case demonstrates the fact that, even with extramedullary tumors located at the lateral aspect of the cord, the symptoms may be entirely of affection of the motor tracts, and the sensory disturbances may be absent for a long period, and when they do appear they may be very slight in intensity. It also illustrates the position which we have taken, that the dura should always be opened, and if a tumor is not present at the point exposed, additional laminæ should be removed, preferably above the suspected site of the tumor, in order to be certain that a neoplasm is not overlooked.

Coincident with the development of paresis, there develops spasticity of the affected limbs.

The reflexes below the level of the lesion are exaggerated in this phase, and the Babinski phenomenon is generally present in the paretic limb. This phenomenon may be present before the appearance of an ankle clonus and even before the development of spasticity. Occasionally, the Babinski reflex is present in both of the lower extremities very early, even before weakness has appeared in both extremities. The presence of reflexes is, of course, dependent upon the localization of the lesion; if the tumor occupies a level which interferes with the reflex arc, naturally the reflex, dependent upon this arc, will be absent. Hence, the condition of the reflexes is a very important symptom for localizing the point where the conductivity of the cord is interrupted.

Delayed micturition or a transient incontinence of urine at this stage is not uncommon.

(3) *Third Phase.*—The symptomatology of this stage is similar to that of a transverse myelitis. The compression of the cord has increased to such an extent that it causes complete paralysis of motor and sensory

functions below the level of the tumor or, as it is sometimes called, *motor and sensory paraplegia*. The paralysis is generally spastic in the beginning and flaccid in the later stages, and, if the compression lasts for a long time, atrophy of the muscles and the electrical reactions of degeneration make their appearance. Flexor contractures develop in the limbs, which are often very painful. Very often there are painful, spontaneous, spasmodic contractions of the lower limbs, such as occur in cases of transverse myelitis. These can often be induced by the application of external stimuli, and the resulting movement of the limbs must not be mistaken for a voluntary muscular effort. They are the phenomena of the defense reaction. There is a complete loss of all forms of sensation below the tumor level. Above this level, there is generally a zone of hyperesthesia. Trophic disturbances, especially bed-sores, develop. The reflexes become very much exaggerated, and a bilateral Babinski is almost always present. Oppenheim's reflex is not as frequently observed as the Babinski reflex. The Gordon and Mendel-Bechterew reflexes may be demonstrated. In some cases, depending upon the site of the tumor and the extent of the compression, the reflexes may be abolished. There may be incomplete retentio:urinæ, or overflow incontinence, or complete incontinentia urinæ. The bowels are usually constipated, although this finally gives way to incontinence.

An unusual symptom in this stage is that of pain in the paralyzed parts, the *paraplegia dolorosa* of Cruveilhier, which is probably due to the compressing tumor causing irritation of the long sensory tracts of the cord. This condition has been noted by Schultze and others, but is not very common.

The development of the symptoms during this phase is usually very slow, and may cover a period of months and even years. On the other hand, the period occupied by the preceding two phases may be very brief, and the beginning of the third phase may come on very rapidly. This is especially true of malignant growths, though the author has seen it in benign neoplasms.

**INTRAMEDULLARY TUMORS.**—It is characteristic of intramedullary growths that they produce early symptoms due to destruction of the integrity of the cord and its functions. The development of these serious symptoms is generally very rapid. Irritative phenomena such as pain and spasms appear, as a rule, only *after* the paralytic symptoms. If the growth lies near the posterior root entrance zone, there may be root pains and symptoms of root irritation, to be followed later by loss of sensation in the areas supplied by the roots, just as in extramedullary growths.

*Pain* has been described by a number of authors, and at times may be extremely severe. Occasionally the pain may be the most prominent symptom of such a tumor over a long period of time. Batten has described a case in which pain lasted for ten months.

The Brown-Séquard syndrome has been observed in cases of intramedullary tumors, though it is unusual. In such cases, the tumor rested in one-half of the cord, compressed the motor tracts on the same side, and interfered with conduction of sensory impulses arising in the opposite half of the body.

The symptomatology of intramedullary tumors depends upon the degree of involvement of the cord structures, both tracts and cells, and a knowledge of the physiology of the cord is necessary, both for the diagno-

sis of the growth and its localization. If the growth involves the meninges, there are symptoms of meningeal irritation added to the clinical picture, and if, as occasionally happens, the vertebral column also participates in the involvement, there may be rigidity and stiffness of the spine, deformity, and marked tenderness on pressure. The motor disturbances are, as we would expect, very pronounced, very extensive, and develop very rapidly. If the growth affects the anterior horn cells or their roots, there are atrophy of the muscles and changes in electrical reaction of the muscles supplied by the segments involved. The functions of the bladder and rectum are interfered with very early, and complete incontinence results. Trophic disturbances such as decubitus and edema are very distressing symptoms. The changes in the reflexes consist either in their exaggeration or their absence, depending upon the location of the growth and its extent.

Intramedullary growths either involve the cord in transverse section very early, or the picture of a transverse lesion may be produced by softening or hemorrhage around the growth. In fact, the early appearance of symptoms of transverse myelitis is quite characteristic of these growths, and the development of this clinical picture, where there is no known infection which could be considered as an etiological factor, should always lead to the suspicion of the possible presence of an intramedullary growth. These growths extend upward and downward in the cord and hence in the beginning they may produce symptoms which are referable to a number of segments.

**Localization.**—The localization of spinal tumors depends upon the exact knowledge of the anatomy and physiology of the spinal cord and its roots. In the interpretation of root-pains and sensory disturbances it is well to bear in mind that each spinal nerve is formed by the union of two roots which arise from the lateral aspects of the cord; the anterior or motor root originates from the anterolateral groove, and the posterior or sensory root, from the posterolateral groove. The motor and sensory roots pierce the sheath of the dura separately, with a thin septum of dura between them. In the cervical region, the nerve bundles remain isolated until they have passed the dura, and are spread out in a fan-like fashion, the broadest part of the fan being at the cord. At their origin, the bundles are spread out so as to occupy 1 to 2 cm. of the cord; between their origin and the dura mater, they are more closely approximated, forming a layer 1 to 1½ cm. in breadth; at the dural perforation, they are still separated from each other. In the dorsal and lumbar regions, however, the individual bundles soon unite to form one bundle, which passes outward to the opening in the dura.

This anatomical arrangement explains the reason why the earliest symptoms of compression of a cervical nerve-root are usually limited to a small area of distribution, one or two fingers, for example, while in the thoracic or lumbar region the root symptoms extend over an entire root area.

It is self-evident that the symptoms produced by tumors vary according to the region of the cord which they involve.

**TUMORS IN THE CERVICAL REGION OF THE CORD.**—The pain may be in the neck, or radiate to the shoulders. If the cervical enlargement is involved, the pain may be in the arms. It may be increased by laughing, sneezing, coughing, or straining at stool, and may be accompanied with some rigidity of the neck.

A tumor in the region of the upper cervical segments may cause dyspnea, and the author has seen such a case, which was treated for asthma for a long time.

Tumors in the uppermost part of the cervical region have been associated with bulbar symptoms. Schlesinger reported a solitary tubercle within the upper cervical cord in which paralysis of deglutition, dysarthria, and salivation began suddenly—and yet microscopic examination of the nuclei of the medulla showed no lesion. Nonne observed a case of intramedullary sarcoma of the upper cervical cord, in which there developed disturbances of deglutition, paresis of both abducens nerves, of the facial, and the masseter muscles, and also an optic neuritis. Stertz has reported a similar condition and found no lesion of the nuclei of the medulla, and no edema. Schlesinger believes that these distant symptoms are due to circulatory disturbances and edema. Nonne considers them due to intoxication. Oppenheim agrees in part with Nonne, and in part with Schlesinger, and he also thinks that the accumulation of spinal fluid above the tumor may exert pressure upon the medulla in such a way as to affect its nuclei, and cause increased irritability. He inclines to Monakow's theory of diasthesis in explanation of the paralysis.

The ascending and descending tracts of the cervical cord form intimate connections between the bulbar and spinal nuclei, and it is easily conceivable that a serious injury to the structures of the upper cervical cord may produce an effect through extension to the nuclei of the medulla, which results in paralysis.

It is important to recognize the fact that tumors in the region of the upper cervical cord can cause bulbar symptoms, in order not to diagnose syringomyelia and syringobulbia, and hence overlook the possibility of the presence of a removable tumor. Oppenheim reports the following case of this type:

CASE IV.—Girl, 13 years old. Increasing weakness in left half of body without pain or paresthesiæ, for a period of five years. Examination showed a typical left hemiparesis spinalis spastica (thumb and fingers of left hand were shorter than those of the right hand), contralateral dissociated sensory paralysis which was marked in the leg only, and homolateral hyperesthesia in the distribution of the upper cervical nerves. There was, in addition, a homolateral paralysis of the vocal cords, paresis of the soft palate, and hypo-innervation of the corresponding facial in its lower branches, besides diminished electrical irritability of the left trapezius. The symptoms pointed to a lesion in the uppermost segments of the cervical cord, on its left side. The only question in the diagnosis was whether the tumor was an encapsulated one pressing on the cervical cord, or gliosis with syringobulbia. Oppenheim states that his early experiences would have led him unhesitatingly to have made the diagnosis of syringomyelia and syringobulbia, but that his later knowledge led him to diagnose a tumor in the upper cervical region which did not extend up to or involve the medulla. He considers the affection of the facial muscle and the left recurrent nerve as having been caused by diasthesis, although, according to the recent work of Rothmann, paralysis of the recurrent nerve may be caused by a lesion in the upper cervical region.

The paralysis in tumors in the cervical region varies in its extent and character, depending upon the segments which are involved; the same

holds true as regards the sensory disturbances. The atrophy of the affected muscles also varies, and is apt to be much more pronounced and earlier in intramedullary than in extramedullary growths, because the pressure exerted by the latter upon the gray matter of the cord is slight and gradual. For the same reason, there may be no changes in the electrical reactions of the muscles, until the growth has existed for some time.

Tumors which affect the cord above the cervical enlargement, even one or two segments above, cause spastic paralysis of the homolateral arm and leg. Very frequently, growths in this region cause paralysis of all four extremities, from the very beginning or early in the course of the disease; this is due to the small circumference of the cord in this region. There are frequently signs of motor irritation in these cases, which are of diagnostic importance. Occasionally there is a paralysis of the diaphragm, which is due to a paralysis of the phrenic nerve. Koeler, Hoffman, Hennerberg, Mundlius, and Oppenheim have observed such cases. The diagnosis has been made by the *x*-ray.

A case has been described in which a tumor compressed the cord at the level of the 3d, 4th, and 5th cervical segments, and produced a hemiplegia spinalis, which was associated with an elevation of the scapula and contraction of the levator anguli scapulæ and rhomboids. In this case the muscles above the level of the lesion were contracted. A growth, affecting the two upper cervical segments, causes an atrophic paralysis of the trapezius and a spastic paralysis of the arm and leg. Eventually, the muscles of the scapula are affected, and there follows a degeneration of the trapezius and subsequently of the sterno-cleido-mastoid muscle. Occasionally the levator anguli scapulæ and the rhomboids are also paralyzed. The area supplied by the highest cervical nerve becomes anesthetic on the side of the growth, and the loss of sensation on the opposite side can extend to the area supplied by the corresponding nerve.

Oppenheim has described a case of an extramedullary tumor, pressing on the upper cervical cord, which was associated with a slight paresis of the lower facial muscles on the same side, and, in addition, with a still slighter weakness of the upper branches of the same facial. This weakness disappeared after the removal of the tumor. A similar case which presented many interesting features of a tumor in the cervical region came under the writer's observation, and is reported below in more or less detail:

CASE V.—L. B., a 24-year-old tailor, was admitted to Mt. Sinai Hospital, on October 2, 1914. Good family, previous, and personal history. Denied lues and gonorrhea by name or symptom. His present illness began two years before admission with a feeling of fullness in the epigastrium, constipation, and nausea, but no vomiting. These gastric symptoms were not relieved by gastric lavage or any other treatment directed to his gastro-intestinal tract, but persisted until April, 1914, when he began to have "sticking" pains in the right acromioclavicular region; these spread within a month to the interscapular region, and to the right shoulder. The pains were unendurable. About the middle of August, 1914, he noticed that during defecation he would have pains in the left side of the small of the back, which would radiate to both iliac regions. After this he began to have "sticking" pains in the inner part of the right and left thighs, and in the middle of the right arm. At about the

same time he began to have a sensation of heaviness in the right forearm, and on and off his right hand would become swollen, the swelling lasting an entire day, and eventually he began to lose the use of that arm. In the left hand he began to experience a "crampy" sensation, with a sensation of cold in the right upper limb. His pain-sense in the right arm was diminished, and he had lost the power of recognizing objects with the right hand. The pain in his legs for the last six weeks was so severe that he was unable to walk, and the sensation of cold extended from the dorsal to sacral regions over the spine. He had lost considerable weight within the same period.

Examination on admission gave the following positive findings:

Pectoral muscles wasted on both sides, more marked on the right, the myotatic irritability of these muscles being markedly increased.

Upper Extremities	Right	Left
Shoulder . . . . .	More curved	Flat
Triceps reflex . . . . .	Marked	Diminished
Biceps reflex . . . . .	Lively	Lively
Fibrillary twitches . . . . .	Marked	Few
Supra- and infra-spinatus muscles . . . . .	Wasted	Wasted
Opponens pollicis . . . . .	Wasted	Wasted
Flexor brevis pollicis . . . . .	Wasted	Wasted slightly
Interossei . . . . .	Wasted	Wasted slightly
Hand . . . . .	Dry and blanched	Dry and blanched
Wrist reflex . . . . .	Absent	Absent
Wrist-drop . . . . .	Present	Present

*Abdomen:* Upper abdominal reflexes, present; middle abdominal reflexes, diminished; lower abdominal reflexes, absent.

*Lower Extremities:* Both knee-jerks increased; bilateral Babinski; weakness of left thigh.

*Muscle Power:* Markedly diminished in left hand and left thigh.

*Gait:* Walks with a rigid spine, which is somewhat scoliosed. Romberg marked.

*Sensation:* Hypalgesia of trunk from second cervical level down to fourth dorsal vertebræ on right side; right arm entirely analgesic; zone of marked hyperalgesia at the level of the fourth dorsal on the right side, and another zone of hyperalgesia, less marked between the tenth and twelfth dorsal on the same side. Temperature-sense diminished from fourth cervical down, but normal on the anterior part of the right leg.

Sense of touch—diminished over the right arm and anterior part of the right chest.

There is also a zone of hypesthesia on the left side between the tenth and twelfth dorsal, and an area of hyperesthesia over the right palm.

Tenderness over 6th and 7th cervical and 1st and 2d dorsal vertebræ; depression of the 1st dorsal and a lateral deviation of 2d to the right.

*Laboratory Findings:* Lumbar puncture yielded 4 c.c. of clear fluid.

Blood and Spinal Fluid—Wassermann: negative.

Urine: trace of albumin.

Temperature: normal.



*Provisional Diagnosis:* Cervical Pott's disease. Plaster cast for immobilizing the neck was applied on October 8, 1914.

Oct. 10, 1914. X-ray showed entire cervical and six upper dorsal vertebræ normal.

Oct. 30, 1914. Condition about the same, except for the appearance of a painful tender swelling of the right hand.

Nov. 6, 1914. Swelling and tenderness of right hand disappeared but pain was still present. Could not flex or extend fingers.

Nov. 14, 1914. Weakness of both hands, cramps in left hand, dull and sharp pains in small of back, markedly constipated.

Nov. 15, 1914. Plaster cast removed. Pains in neck, less severe.

Nov. 16, 1914. Severe pain in both upper extremities, more marked in the right. Pain over lower cervical spine on movement.

Nov. 29, 1914. Patient had a sensation of cold over the entire spine. Severe pains in the left chest and in both palms.

Dec. 11, 1914. Increased weakness and atrophy of both hands, weakness of the muscles of the back, pectorals more wasted, spastic ataxic gait more marked on the right side. All abdominal reflexes absent, cremasterics present but diminished. Was able to raise both arms. Right biceps group weaker than left; right lower extremity much weaker than on admission. Both knee-jerks exaggerated, but more marked on the right side. Right plantar reflex markedly exaggerated; left lively. Distinct ankle clonus on right side. Right Achilles livelier than left. Bilateral Babinski. Sensory changes—about the same as on admission.

Dr. Sachs, who examined the case at that time, was of the opinion that, because there was a predominance of symptoms on the right half of the body, the lesion was probably focal in nature—a neoplasm rather than tuberculous spondylitis.

Dec. 12, 1914. All muscles of the shoulder, arms, and hands, including the interossei, reacted promptly to both faradic and galvanic electricity. X-ray showed absorption of transverse process of 6th and 7th cervical.

An orthopedist, who saw the case at this time, made the diagnosis of "A chronic inflammatory process in various parts of the spine."

Dec. 28, 1914. Pains in the left lumbar region and abdomen, and right leg. Patient was losing weight. Unable to walk on account of the severe pain in both legs.

Jan. 2, 1915. Lumbar puncture yielded about 10 c.c. of canary-colored fluid under considerable pressure. Examination showed serum albumin and blood-fibrin, but no blood-pigment present as such. Xanthochromic (Nonne-Froin) reaction.

Jan. 3, 1915. Marked zone of hyperesthesia about the right buttock in the distribution of the 3d, 4th, and 5th sacral. Left side of body hypalgesic; right, normal except for area of hyperalgesia around 4th dorsal, and another around 10th and 12th dorsal. The sense of temperature was diminished from 4th dorsal down.

Jan. 7, 1915. Patient unable to walk at all.

Feb. 16, 1915. Tenderness over cervical and dorsal spine. Marked wasting of entire musculature of both arms, with exaggerated reflexes and paralysis. Joints, flaccid and loose. All abdominal reflexes absent. Cremasterics absent. Knee-jerks and Achilles jerks exaggerated. Bilateral ankle clonus and Babinski; right lower extremity totally paralyzed. All forms of sensation diminished from 4th cervical down. Left leg, total anesthesia. Retention of urine.

Feb. 19, 1915. X-ray—moderate degree of arthritis in the cervical vertebrae; bodies of 3d, 4th, and 5th cervical vertebrae showed moderate absorption.

Feb. 26, 1915. Transferred to the service of Dr. Elsberg for an exploratory laminectomy. At operation, an extramedullary subdural tumor was found in the upper cervical region of the cord, which was removed without difficulty. The operation was followed by marked improvement, both as regards the pain and power in the paralyzed extremities.

Jan. 15, 1915. Patient admitted to the neurological wards of the Montefiore Home and Hospital, where he has been continually under our observation. Although he complains of occasional stiffness in the neck and a sense of constriction and burning in the upper part of the chest, his general condition has markedly improved, and he is up and about, and quite comfortable.

April, 1919. Patient discharged from Home. He has a remaining atrophy and weakness of both hands. The power in his upper arms and legs is excellent.

In tumors of the upper part of the cervical enlargement, the paralysis of the arm is apt to be an atrophic one. The leg is spastic, although this is not always the case. If the tumor is situated in the upper part of the enlargement, there may be an atrophic paralysis of the muscles of Erb—the deltoid, biceps, brachialis anticus, supinator longus, and occasionally the supinator brevis and infraspinatus. The lower arm flexor reflex is absent. When the styloid process of the radius is tapped, instead of normal flexion of the forearm, there is a flexion of the fingers (Babinski). The triceps reflex is generally increased. The muscles, which receive their innervation from the lower portion of the cervical enlargement, are weak and become spastic.

Tumors of the lower part of the cervical enlargement, especially those involving the 8th cervical and 1st dorsal segments, cause an atrophic paralysis of the small muscles of the hand. The triceps is also generally involved, the triceps reflex being then absent. The supinator reflex, flexor reflex of the arm, and pronator reflex are present and may be exaggerated. There is a spastic paralysis of the leg on the same side, together with the Babinski and Oppenheim phenomena.

The oculopupillary symptoms (contractions of the pupil, narrowing of the palpebral fissure, enophthalmos, etc.) are present on the side of the lesion. Contralateral anesthesia of the leg and trunk develops; also homolateral anesthesia of the lower root region of the arm. The paralysis may affect muscles which are innervated from neighboring segments. The tumor may be elongated and cause injury to almost the entire

cervical enlargement, so that a degenerative paralysis of all the muscles of the upper extremity, with loss of all tendon reflexes, may occur.

CASE VI.—A. W., 28 years of age. Married.

Stiff neck six weeks, pains in left arm four months.

Attack of influenza January for three weeks. No other acute illness.

About four months ago he began to suffer from drawing pains beginning at the wrist, extending upward along the anterior surface of the arm to the shoulder. These pains were described as drawing and were associated with feeling of tightness and contractions in the muscles. Up to the time patient had influenza these pains were not very severe, and dur-

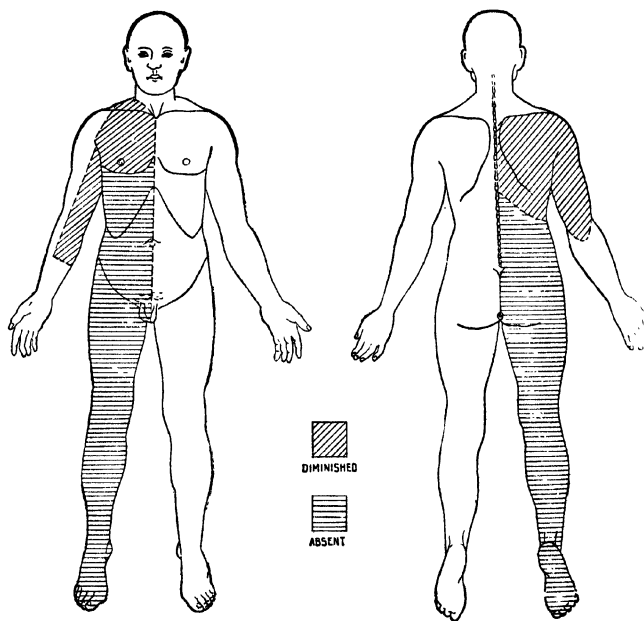


FIG. 5.—CHART OF THERMAL SENSATIONS IN CASE VI. (A. W.)

ing the attacks he was completely relieved. Immediately following the influenza, pains recurred and have been constant since. About six weeks ago these pains extended to the back of the shoulder and up the back of the neck. Any movement of the neck is painful, so as to make him keep neck in a stiff position. No paralysis of extremities, but definite weakness. For past two weeks has had burning sensation over right upper and lower extremities. For past week has had difficulty in emptying bowels. Bow-

els feel full, but it is impossible for him to pass feces. For three days has had difficulty in beginning urination, but once started, empties bladder easily. No incontinence. For three days swallowing has been painful and causes irritation in the back of the neck. No fever, no headaches, no visual disturbance.

*Physical Examination.*—Well developed, well nourished, not acutely ill, complaining of pain in neck radiating down both arms.

*Head:* No tenderness, tilted slightly to the left with chin to right.

*Eyes:* Pupils equal, regular, central, react to light and accommodation. No palsies, fine nystagmus on looking to the right.

*Face:* Slight left facial weakness, jaw-jerk lively.

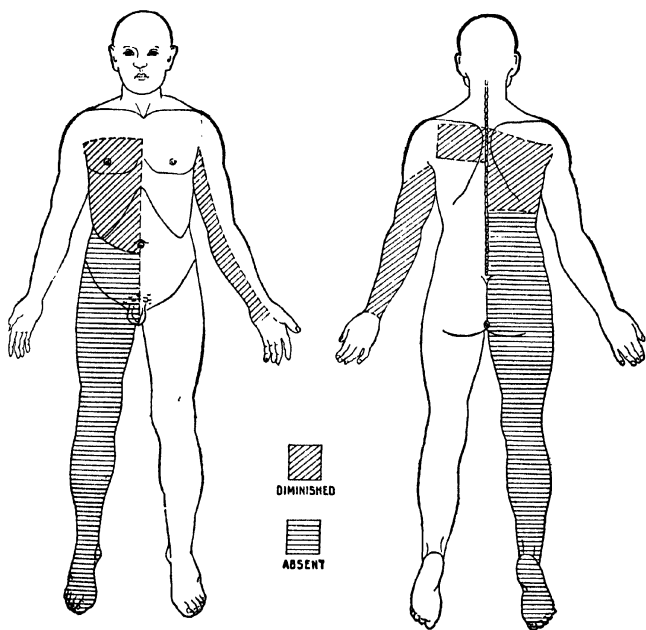


FIG. 6.—CHART OF PAIN SENSATION IN CASE VI. (A. W.)

*Chest:* Unsymmetrical due to wasting of left pectoral muscle, irregularity of clavicle.

*Extremities:* Power unequal, right grip much stronger than left, marked wasting of left upper extremity most marked around shoulder girdle. Pectorals, trapezius, supra- and infra-spinatus, and rhomboids show wasting. There are flattening about the shoulder joint, moderate wasting of the muscles of the arm and forearm. Flattening of thenar

and hypothenar eminences. There is lack of normal contour of the left hand. Left extremities somewhat cyanotic. On right side there is slight trapezius wasting. Reflexes on right side exaggerated. Lower extremities show no wasting. Power slightly greater on right side. Left knee-jerk exaggerated, left ankle-jerk also exaggerated. Exhaustible ankle clonus on left side, none on right.

*Back:* Tenderness over upper cervical vertebræ. Fullness over right side posteriorly in mid-cervical region due to spasm of muscles.

Slight trace of weakness of left side. Slight tremor of left hand, exaggerated by intentional movement and by pointing to the right. No adiadokokinesis.

*Gait:* Tendency to stiff gait, especially on left side.

*Attitude:* Rigidity of neck. Right shoulder sloping to a lower level than left.

*Sensorium:* See Charts (Figs. 3 and 4). Some loss of joint and muscle sense of left upper extremity.

*Reflexes:* Left abdominal absent, left cremasteric absent.

April 7. Lumbar puncture. Fluid under slight increased pressure; 4 cells, normal color. Wassermann of fluid and blood negative.

April 10. On holding hands forward, distinct atrophy of rhomboids and infrapinatus on left side. Inability to bring chin on chest; when he attempts to do this, chin points to the right. Marked limitation of movement backward. Right reflexes present, left diminished. Grasp of left hand weak. Possibility of cervical lesion compressing roots. Nature of process undetermined. Lues or neoplasm.

April 13. Patient constantly complains of severe drawing pain in neck down both shoulders and arms. No change in neck than those previously observed. Left arm and hand somewhat more cyanotic, power very weak and limited by pain. X-ray examination of the cervical spine fails to show any irregularity or deformity of the vertebræ.

April 19. Plaster cast to support neck and chin, with much relief of subjective symptoms.

April 20. Pain down arms caused by swallowing, laughing, etc.

May 3. Plaster cast removed. Marked weakness of left arm with marked wasting of interossei. Tenderness over 4th and 5th cervical vertebræ. Reflexes of left arm markedly diminished.

Marked narrowing of left palpebral fissure, with slight enophthalmos and inequality of pupils—right greater than left, right being normal.

Extramedullary neoplasm in region of 4th and 5th cervical vertebræ.

May 8. Symptoms point to lesion of 4th and 5th cervical region, probably extramedullary. Operative interference advised.

Pain in left arm progressively increasing, especially at night. Increasing doses of narcotics necessary to permit sleep.

May 10. Operation by Dr. Elsberg. Extramedullary tumor, the size of a lima bean, removed in the region of the 4th and 5th cervical roots on the left side. Tumor was a fibroma.

Uneventful recovery.

The following case illustrates that, although the x-ray showed spondylitis of the cervical spine, and although the patient had a palsy of the recurrent nerve and oculopupillary disturbances (rare for a tumor of the

cord), the involvement of the motor tracts, without marked sensory disturbances, spoke in favor of a cord tumor as being the probable cause of the patient's condition:

CASE VII.—L. W., a 59-year-old married man, was admitted to Mt. Sinai Hospital on March 15, 1913. His family history was negative. Past history showed that he was a heavy drinker and smoker, and had had gonorrhea in youth, but denied syphilis by name or symptom.

Present illness began five months ago with paresthesiæ in the arms and legs; no chills or fever. The patient had numbness and weakness in both legs; the weakness was progressive, and one and a half months before admission his legs became so weak that he could not support himself. At this time, his left upper extremity also became weak. He frequently felt a sense of constriction about the waist line. Although he passed urine frequently, he had no incontinence. He had lost considerable weight.

Examination revealed the following positive findings: Second aortic sound accentuated; liver enlarged (edge sharp and hard, and felt three fingers below free border); right pupil greater than left, both reacted sluggishly to light; upper right extremity, normal; upper left extremity—muscles of arm, forearm, hand and interossei (especially those of the first interosseous space)—atrophied; there was also marked weakness in this extremity, with fibrillary twitchings; reflexes present. Abdominal reflexes much diminished, especially on the left side; slight diminution of pain and touch sense below the 5th rib on the left side, including the left leg; over left upper chest, there is some perversion of heat and cold sensation; lower extremities—power good, no atrophies, right knee-jerk diminished, both Achilles present and equal, no clonus or Babinski.

March 20, 1913. Marked atrophy of the opponens and interossei of the left hand. Left wrist and finger-jerks exaggerated, typical "main en griffe" with ulnar deviation of little finger. Lateral curvature of the spine with convexity to the right. Flattening of left chest. No tenderness over spine. Abdominals not elicited. Bilateral Babinski; exhaustible ankle clonus. Crossed adductor reflexes on both sides present.

March 24, 1913. Lumbar puncture yielded a slightly greenish fluid under normal pressure. Wassermann and cytology of the fluid were negative. Wassermann of blood, also negative. Sensory disturbances, same as on first examination.

March 28, 1913. Patient was complaining of pain, burning and tearing in character, in the left shoulder and radiating to the left arm. The pain was so severe that he was unable to sleep. An x-ray examination showed spondylitis of the 2d, 3d, 4th and 5th cervical vertebrae.

March 31, 1913. Slight cervicodorsal scoliosis; atrophy of left trapezius, deltoid, infraspinatus, serratus, rhomboids; atrophy of the muscles of the left hand with fibrillary twitchings of the left forearm. Wrist reflexes present and not exaggerated. Severe pain in left shoulder.

April 7, 1913. Left knee-jerk exaggerated; right normal. Marked bilateral ankle clonus; bilateral Babinski; muscular excitability on the left side of body increased; gait spastic—paretic; patient staggered while walking; left leg very weak. Without support with the upper extremities, he was unable to raise his body from the bed. The muscles of the left side of the abdomen appeared wasted and of diminished tone.

April 8, 1913. Laryngologist reported: Left recurrent laryngeal paralysis; entire left side of larynx paralyzed; left false cord seems tumefied.

April 11, 1913. Weakness of left leg more marked. Severe pain in left shoulder.

April 17, 1913. General condition of patient fair; pain not so marked. Unable to walk at all; left leg completely paralyzed, right leg paretic. No other sensory disturbances, except an area of hyperesthesia over upper part of chest.

May 9, 1913. Exploratory laminectomy (Dr. Elsberg) revealed soft tumor overlying the 4th to 6th cervical segments. Dura did not pulsate. Tumor was removed. After the operation the patient experienced a rather stormy convalescence, and on June 9, 1913, with no change in the neurological status, the patient expired as a result of general asthenia. On examination tumor proved to be a sarcoma.

A circumscribed growth which is accompanied by meningitis serosa or a pachymeningitis of considerable extent may cause the same extensive symptoms.

**TUMORS OF THE THORACIC CORD.**—Growths in this region may exist for a considerable period without giving any symptoms other than those of the first phase. The pain is frequently that of an intercostal neuralgia. If the lower half of the cord is affected, the pain may be referred to the abdomen and be mistaken for gall-bladder or renal colic. Unless examined very carefully, the slight sensory changes dependent upon the involvement of the roots can be overlooked and the patient treated for a functional condition. It may be necessary to observe such a case for a long period until the first symptoms of cord compression make their appearance.

There may be a girdle sensation around the chest or the abdomen. In the early stages the author has met cases where the sensory disturbances did not as a rule extend below the ankle. The feet, both dorsal and plantar surfaces, very frequently do not show any sensory disturbances. (This fact has also been noted by Frazier.) The sensory disturbances below the level of the lesion consist first in the loss of pain and temperature sense on the side opposite the growth. The sensation of touch may also be diminished in the same region, and occasionally a slight diminution of the sensibility of touch may be found on the same side as the lesion. This, however, cannot be made out unless a very careful sensory examination is made. As noted before, the dorsal and plantar surface of the feet as a rule fail to show sensory disturbances unless the compression of the cord has existed for a considerable length of time.

Very frequently above the level of the lesion there is a zone of hyperesthesia. This zone may be on the side of the lesion, or it may involve both sides. The author has frequently noticed that the zone of hyperesthesia is more marked on the posterior surface of the trunk than on the anterior surface. If the compression of the cord is considerable, due either to the long-standing pressure of the growth or to sudden hemorrhage or edema in the cord, the loss of sensation on both sides of the body below the lesion becomes complete, as in transverse myelitis. Occasionally, if the tumor is situated on the posterior aspect of the cord, there is not only loss of the deep pressure sense which may involve both limbs.

but also an ataxia of the lower extremities; and this may result in a staggering gait and a marked Romberg.

Nonne, Schultze, Auerbach and Brodnitz have described cases of tumors in the thoracic region where the Brown-Séquard syndrome apparently was not present, and the symptoms of severe compression of the cord made their appearance very early. It is possible, however, that had these cases been observed carefully at an early stage, a Brown-Séquard syndrome would have been found. As a rule the paralysis of the contralateral leg is spastic in nature. There may, however, be demonstrated a slight weakness of the homolateral leg, even in the early stages of compression. If the tumor causes marked compression of the cord, the spastic paralysis may become flaccid, and later on there may occur flexor contractures in one or both lower limbs.

Occasionally the muscles of the paralyzed limb show a slight degree of atrophy—especially when the compression is of long duration. In such cases changes are found in the electrical reactions of the muscles. The trophic disturbances, such as glossy skin, or vasomotor disturbance, such as coldness and paleness of the paralyzed extremities, may be present. At times the abdominal muscles upon the side of the growth are paretic. Oppenheim describes a case of tumor in the region of the 8th and 9th dorsal vertebræ, which caused atrophy of the abdominal muscles.

The deep reflexes of the paretic limb are exaggerated early, and the Babinski and Oppenheim phenomena, with ankle clonus, are present. Later on, the Babinski sign may appear in the homolateral limb before marked weakness of this limb can be demonstrated. The abdominal reflexes vary with the localization of the tumor. If the tumor is up in the mid- or lower thoracic region, there may be, in the early stages, an absence of the abdominal reflexes, both upper and lower. Later on, all abdominal reflexes may be absent. The abdominal muscles occasionally are rigid.

Very often the spinous processes overlying the neoplasm are tender. Percussion over the tumor has on one or two occasions yielded a definite dull note.

The bladder symptoms in the early stages of these tumors are very slight; later on, the patients usually complain of a slight delay in micturition.

**TUMORS OF THE LUMBAR AND SACRAL CORD.**—The differential diagnosis of tumors affecting the lumbar cord and the cauda equina is very difficult because a growth in this part of the vertebral canal can compress both of these structures and produce practically the same symptoms. Tumors in this region, because of the size of the vertebral canal, may also grow to a considerable size before they cause definite symptoms of compression.

The symptoms are generally those produced by compression of the roots. The pain is frequently very severe and radiates into the hips and the lower spine or along the course of the sciatic nerve; this pain is often wrongly diagnosed and treated as sciatica. The pain in these cases is greater than that caused by tumors affecting any other portion of the spinal canal. Sensory symptoms may be present and prominent for a long time before there are any motor symptoms. Frazier thinks that this is due to the fact that the sensory roots are larger than the motor ones. The symptoms in the beginning may be unilateral. The anesthesia is characteristic of root compression and affects all forms of sensation; it conforms to the areas of the skin supplied by the different roots. As a



rule, there is diminution of reflexes, and very soon loss of the same. The reflexes which are lost depend upon the site of the neoplasm and its relation to the roots or segments of the cord through which the respective reflex arcs pass.

As stated above, the motor symptoms may be very slight in the beginning, and very late in their appearance. The paralysis is an atrophic flaccid paralysis, such as one would expect from a lesion affecting the anterior roots; reaction of degeneration is therefore very common.

Occasionally, tumors in this region produce visceral anesthesia and also disturbances of menstruation.

The function of the bladder and rectum is interfered with very early. An exception to this is found in the cases of the large cauda equina tumors, described by Collins and Elsberg, in which, although the tumors filled the entire lower portion of the vertebral canal, vesical and rectal symptoms did not appear until later in the disease; the sensory disturbances were very slight and also appeared very late. The hypogastric plexus of the sympathetic nervous system contains centers which exercise a very important control over bladder function, and it is possible that these centers functionate in these cases, even though the roots of the cauda equina are extensively involved. Oppenheim divides the tumors of this region into four groups:

*First:* Tumors at the level of the 2d lumbar vertebra, which involve the entire cauda equina, causing atrophic paralysis of the bladder and rectum, impotence and loss of reflexes.

*Second:* Growths between the 3d and 5th lumbar vertebræ causing atrophic paralysis and anesthesia in the distribution supplied by the sciatic nerve. The patellar and cremasteric reflexes are usually present.

*Third:* The lesion from the 5th lumbar to 2d sacral vertebræ, the sciatic nerve being partially affected.

*Fourth:* The lesion below the second sacral vertebræ causing no paralysis of the lower extremities but an isolated vesical and rectal paralysis, incontinence and perianal genital anesthesia in the characteristic horse-shoe-shaped or "saddle-shaped" area.

The following case is illustrative of a typical case of a tumor of the cauda equina, particularly as regards its long duration, the severity of the pain and the mild nature of the objective symptoms at the beginning of the disease:

CASE VIII.—H. R., 60 years old, was admitted to the private pavilion of the Montefiore Home and Hospital on February 12, 1918. His previous and personal history has no bearing on the case.

His present illness began twenty years ago with a sudden "paralysis" of the right lower extremity. This "paralysis" (this was apparently only a weakness) was accompanied with repeated attacks of excruciating pain in the affected limb, which was occasionally somewhat relieved by the application of any form of heat. He consulted many physicians during these twenty years, but no satisfactory diagnosis was made.

Two years before admission, he was operated on for a double inguinal hernia, from which he had been suffering for the last ten or twelve years. Since that operation, the whole left lower extremity became gradually involved in the same way as the right one; occasionally he also had pain in the region of the lumbar and sacral spine. The pain in the lower extrem-

ities was irregular in distribution, radiating occasionally from the lumbar region downward along the distribution of the anterior crural and sciatic nerves. His gait was interfered with only when he had an attack of pain. There was never any loss of weight or edema in any part of the body.

The general physical examination, aside from a systolic blood-pressure of 155-160, a small dermoid growth on the upper part of the outer side of the right thigh, and an enlarged, soft prostate, was negative.

The neurologic examination showed the right lower extremity to be slightly hypotonic. There was no evidence of muscular atrophy any-

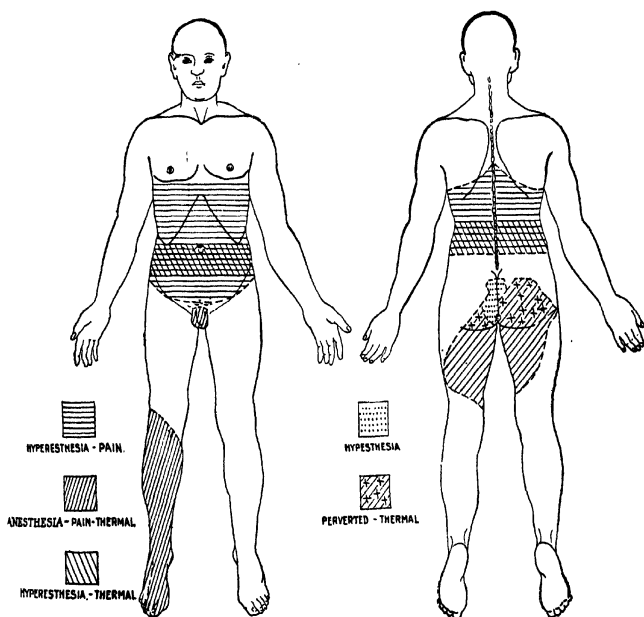


FIG. 7.—PAIN AND THERMAL SENSATIONS IN CASE VIII. (H. R.)

where. The spine showed no deformity and there was no pain or tenderness on palpation or on deep percussion.

The superficial and deep reflexes in the upper part of the body were normal. The upper and lower abdominals were very lively; the cremasterics, knee-jerks and ankle-jerks were absent on both sides; there was no clonus and no Babinski, Oppenheim or Chaddock.

The sensory examination showed a belt-shaped area of hyperesthesia in the distribution of the 7th and 12th dorsal anteriorly, and 5th and

10th dorsal posteriorly. This area of hyperesthesia was more pronounced in the upper half of this "belt" area than in the lower half; there was complete analgesia on the anterior surface of the right leg, beginning somewhat above the knee, and on the dorsal surface of the right foot, except for a small area corresponding to the distribution of the 5th lumbar. There was also analgesia of the whole right buttock and posterior surface of the left thigh; the middle third of the left buttock was hypæsthetic, while on the inner third of the same buttock there was at times analgesia, alternating with hyperesthesia.

There was a belt-shaped area of increased sensibility to hot and cold, corresponding anteriorly and posteriorly to the areas of distribution of the 10th and 12th dorsal.

There was a complete absence of the temperature sense in the penis, scrotum, anterior surface of the whole right leg beginning somewhat above the knee, the whole right buttock, the posterior surface of the right thigh, the middle third of the left buttock, and the greater part of the posterior surface of the left thigh (sacral 1st and 3d; lumbar 3d, 4th and 5th anteriorly, and lumbar 1st, 2d, 3d and 5th; sacral 1st, 2d, 3d, 4th and 5th posteriorly). In the inner third of the left buttock the temperature sense was perverted (sacral 4th and 5th).

There was a complete loss of the sense of touch over the penis, scrotum, the inner two-thirds of both buttocks, and the upper two-thirds of the posterior surface of both thighs (sacral 3d, 4th and 5th).

On February 18, 1918, the examination showed, in addition to the above findings, a weakness of the flexors of the left foot, with a slight atrophy of the anterior muscles of the left thigh.

Cerebrospinal fluid was under increased pressure and contained an excess of globulin, numerous cells and a marked xanthochromic reaction. Wassermann, negative in the blood and cerebrospinal fluid.

The urine was of a specific gravity of 1.025–1.035, and showed a marked trace of albumin, with a few hyaline and occasional epithelial casts. No sugar present.

X-ray examination showed very marked arthritic changes between the lower 4 dorsal vertebræ, and slight arthritic changes throughout the lumbar vertebræ. There were no evidences of any gross bony changes or of any destructive process in the sacrum.

On February 21, 1918, under ether and gas, Dr. Elsberg removed the arches of the 12th dorsal and first and second lumbar vertebræ; there was a moderate hemorrhage. An incision into the dura, which was found to be very thin, was followed by an escape of considerable yellowish fluid and a tumor, the size of a prune, was found filling up the spinal canal. The tumor was well encapsulated and was closely connected with numerous nerve-roots. In the removal of the tumor, several nerve-bundles had to be divided, others could be dissected off from the tumor capsule. The tumor was removed in two pieces. There was rather free hemorrhage, requiring ligation of two small vessels. The conus could not be seen. After controlling the bleeding, the wound was closed in the usual manner.

Examination of the tumor showed it to be an endothelioma.

**TUMORS OF THE CONUS MEDULLARIS.**—These tumors do not cause paralysis unless they grow to such an extent as to compress the roots of the

cauda equina; pain in these cases is a prominent symptom. The anesthesia affects the penis, scrotum, perineum, anus, the inner aspect of the buttocks, and the posterior aspect of the thighs. Jacobsohn shows graphically the most common differences between conus and cauda lesions, in the following table:

CONUS	CAUDA
1. Pain lacking or slight.	1. Violent pain in the sacrum, perineum, and lower extremities.
2. Sensory disturbance frequently dissociated.	2. Sensory disturbance almost never dissociated.
3. Motor disturbance most prominent symptom.	3. Motor paralysis lacking, or appearing only late.
4. Paralysis and sensory disturbance distributed symmetrically.	4. Disturbances less symmetrical.
5. Achilles reflex lost, patellar sometimes increased.	5. Achilles reflex lost, patellar diminished.
6. Tendency to decubitus and trophic disturbances.	6. Less tendency to decubitus and trophic disturbances.

Paralysis of bladder and rectum appears very early. The anesthesia, as a rule, makes its appearance shortly after the affection of the bladder or rectum, but it may appear at about the same time. Trophic disturbances also make their appearance very early. The anesthesia is usually bilateral; if unilateral, it indicates an involvement of the conus and cauda, or more often of the cauda alone.

There are certain criteria in the differential diagnosis as to whether the tumor is located in the conus or the cauda, but these are not always reliable. According to L. R. Muller, the following points of differential diagnosis are important:

In favor of disease of the cauda is the slow development of symptoms: severe pains which are shooting and spasmodic in character, pains radiating into the bladder and along the course of the sciatic nerve, and later the appearance of anesthesia for all forms of sensation. There is an absence of irritative motor phenomena, and following the period of pain there may be a gradual development of paralysis and likewise a disturbance of sexual power, bladder and rectal innervation.

A disease of the conus is characterized by its rapid development; almost always there is complete absence of pain, very early appearance of anesthesia which may be of a dissociated character, motor irritative phenomena such as fibrillary twitchings and involuntary spasms, and a general and rapid development of paralysis of the bladder, rectum, and of the intestinal musculature according to its segmentary innervation; very often there is persistent erection. In addition, Bruns and Cassirer have called attention to the asymmetry of the symptoms in conus lesions. In favor of disease of the cauda there may be tenderness of the 2d lumbar vertebra, rigidity of the lower vertebral column, remissions in the symptoms, and improvement of the bladder and rectal functions.

These points of differentiation of the two conditions may often be of value, but in some cases differentiation may be absolutely impossible. Pain, the most prominent symptom of cauda tumors, may occasionally be absent, as in one of Volhard's cases. Cases have been reported in which the pain had been present but disappeared, and remained absent for a

long period. Kleinberger has reported a case in which the pain first appeared on the soles of the feet, disappeared for a period of two years, then returned, and disappeared again, after which the typical picture of a tumor of the cauda equina was observed.

**Diagnosis.**—**DIFFERENTIAL DIAGNOSIS.**—The diagnosis of tumors of the spinal cord and its adnexa requires careful study and repeated thorough examinations. In every case, several important questions must be answered: (1) Do the symptoms point to a neoplasm or to some other spinal or nervous disease? (2) If the symptoms point to a neoplasm, what is its exact localization? Does it arise from the cord, its roots, the meninges or the bones? (3) What is the nature of the tumor; is it single or multiple, or diffuse; is it primary or secondary? (4) Is it malignant or benign?

In the differentiation from *spinal syphilis*, it is well to bear in mind that, although gummata may act on the roots and cord like any other neoplasm, they do not show the steady development and progressive course that the latter do. The tendency to a sudden onset with sudden exacerbations and remissions is more common in gumma. The symptoms of syphilis of the spine are usually those of *multiple* lesions at various localizations of the cord and brain. Of course the history of a luetic infection together with the examination of the blood and cerebrospinal fluid will be of great diagnostic aid, as will the results of energetic anti-luetic treatment.

Localized deformities of the spinal column point to the presence of a primary spinal tumor, which is generally malignant if caries can be excluded, although endovertebral hydatid and other cysts or aneurysms may, by eroding the bodies of the vertebræ, produce deformities. Vertebral tumors are usually secondary, and the history of another growth in a different part of the body will indicate the true nature of the disease.

The first symptom of *carcinomatous metastasis* of the spine is usually pain; this is persistent and spontaneous and in a case where the primary growth has been discovered, should always lead to the suspicion of a metastatic process. In the beginning there is very little tenderness of the vertebræ, although motion of the spine may intensify the pain. Schlesinger, as well as Bruns, Litten, and Oppenheim, have called attention to the fact that bone pain may be absent in vertebral growths whereas the root and cord symptoms may be the first symptoms present. Skversky and Petran have both called attention to the fact that it is sometimes very difficult, because of the deep-seated, changeable, and unlocalizable character of the pain, to determine whether it is of root or bone origin. The root pains, due either to pressure by the growth upon the roots or by their inflammation, become the predominating feature of the clinical course. Bruns has called attention to the fact that very frequently the pains are bilateral, and that this bilaterality is to a certain extent symptomatic of carcinoma of the spine. Spinal deformity is usually absent. The deformity differs from that of *spondylitis*; in fact, it is rounded rather than angular. There may be rigidity of the vertebral column sooner or later. Compression of the cord with subsequent paralysis, both motor and sensory, develops in the later progress of the growth. Early in the development of the metastasis, the x-ray unfortunately fails to reveal any pathological change in the bone. When, as sometimes happens, the carcinoma

has produced considerable destruction of the bodies of the vertebræ, the roentgenographic findings are of great assistance in the diagnosis.

The following case of *adenocarcinoma of the thyroid with metastasis of the spine*, reported by Skversky, is interesting in showing the difficulties met with in diagnosing these conditions when the primary growth is unrecognized:

CASE IX.—B. K., male, age 52, was admitted to the Montefiore Home and Hospital on December 16, 1915, complaining of pain in both hips, radiating down the legs, so that he was unable to walk for any distance. He was a brass worker, married, no children; his wife had no history of miscarriage; venereal or previous illness denied.

Present illness, which dated back two years prior to admission, began with cutting pains in the left lower limb, commencing above the pelvis, and radiating down the inner side of the ankle. He used various remedies without relief. About six months later he began to experience similar pains in the right lower limb. He was placed in a plaster-of-Paris jacket for about six months, but was not relieved of his pain, although he stated that his spine, "which had been lame, straightened out." The pain which was very severe was not constant or definitely localizable, but mostly in his legs and ankles, never in his feet. While in bed, he found comfort only when lying down on either side; turning over was accompanied by sharp pains in the back of the pelvis. There was no pain upon urination or defecation.

On admission, examination revealed an elderly male, appearing much older than the age given, rather obese and anemic. He was able to walk slowly and guardedly, with the aid of a cane, but while on his feet he appeared to be suffering severely from pain. His head and cranial nerves were negative. Examination of the neck did not reveal any thyroid enlargement; no abnormal masses were felt, nor was there any apparent enlargement of the regional lymphatics. Heart and lungs were negative. His abdomen was protuberant with a heavy panniculus; no tenderness, and no masses could be felt. Genitals, negative. Extremities: upper, negative; lower, all active movements present and unrestricted. Passive movements of left limb met with some resistance, but there was no tenderness of the nerve trunks. The right knee-jerk was lively, the left much diminished and occasionally extremely difficult to elicit. No Babinski or clonus; no sensory, vasomotor or trophic disturbances. Examination of the spine did not reveal any deformities, rigidity, tender areas or alterations in consistency.

Blood, urine, and serology were all negative.

In the absence of objective organic features, the case was, for the time being, considered to be probably of a functional nature, and held for further observation.

January 25, 1916. Pains vague and irregular, at times severe and again frequently absent. All difficulty was apparently centered in the region of the sacrum and in impaired locomotion. On standing, there was no spinal deformity, but on bending, the lower part of the back gave the impression of being flat and rigid. Extremities presented no atrophies and all movements were unhampered. The patient stamped vigorously with both heels without complaining of pain. Upon rotation of the

lower spine, there was intense pain in the sacral region, radiating downwards in a general manner along the course of the sciatic nerve on the right more than on the left. Heavy percussion over the sacrum and all rotary movements, involving the lower spine, elicited marked pains. The abdominals and cremasterics were present and equal; the right knee-jerk was lively, the left barely obtainable on reinforcement; both Achilles-jerks diminished; no Babinski, ankle clonus, or sensory disturbances. The prostate felt enlarged and somewhat harder than normal, but not tender; its outlines were not determined. At this time the condition was considered to be one of osteitis of the sacrolumbar spine, and an x-ray examination was advised. The roentgenologist reported slight evidence of a defect in the outlines of the left border of the body of the 4th lumbar vertebra, but added that this was probably an artefact and of no significance.

The patient was given electric-light baths, followed by vibratory massage to the left hip and thigh, three times a week, for two months, and while no special effects were observed, the patient on several occasions, when questioned, stated that his pains were generally less severe, and that he was, at times, even free from pain.

April 16, 1916. Patient began to suffer from excruciating pains in both hips and lower extremities, and took to his bed. Examined by Dr. I. Strauss, who noted that the left knee-jerk was absent, and advised that another roentgenogram be taken. Pains became more intense, the patient shrieking spasmodically upon slight movements, and not responding to opiates. He was able to move the left lower extremity to a very slight degree; movements in the right, unhampered. Passive flexion and rotation of both thighs, especially the left, produced marked pain.

The roentgenologist, on April 20, 1916, reported bone defect, involving the left half of the body of the 4th lumbar vertebra, also small contiguous portions of the 3d and 5th vertebrae. He now suggested a tumor as the possible cause.

The patient developed acute retention of urine and feces; his abdomen became distended; required very drastic catharsis after failure of enemata, and catheterization, with ready entrance into bladder, yielded large quantities of urine. The prostate felt enlarged but soft, and did not suggest malignancy. He began to show evidence of rapid loss of weight, and a peculiar yellowish cachexia. Examination of the spine showed no evidence of deformity or tumor mass. There was extreme tenderness on pressure over the 3d, 4th and 5th lumbar spines, especially on percussion; also tenderness over both sacroiliac regions, more on the left.

The pains continued much the same as described, but with increased intensity. There developed some edema and a definite drop-foot on the left side, but no gross evidence of muscular atrophies, the edema interfering with the determination of the electrical reaction. The left knee- and Achilles-jerks were absent; no plantar response; the right knee-jerk was brisk, and the right Achilles-jerk could not be elicited, but there was a tendency to voluntary dorsal extension of the right big toe, with an occasional suggestion of a Babinski.

Sensory examination now revealed anesthesia, analgesia, thermanesthesia with some perversion over the region from the L 5 to and including the S 5 on the left side, quite sharply defined. At the beginning of the

anesthetic area, there was complete loss of postural sense in the left lower extremity. The right showed no sensory disturbances.

The clinical diagnosis now established was malignant disease of the spine, probably secondary to the prostate, although the latter did not reveal the characteristic feel of malignancy, but rather of a mass behind it. Sacral decubitus developed rapidly, and after a comatose state of about twenty-four hours, the patient died on May 6, 1916.

*Pathological Findings.*—Autopsy was performed forty hours after death, by Dr. B. S. Kline. The body was that of a well-nourished individual with an abundant panniculus; skin of good color.

Both lungs presented evidence of a diffuse bronchopneumonia. None of the thoracic, abdominal, or pelvic organs revealed any malignant disease. Just outside the capsule of the left adrenal, and also imbedded in the surrounding fatty tissues, were two small grapeseed-sized masses, which proved to be accessory adrenals. The prostate was of average size and consistency, with no evidence of disease. The rectum was surrounded by a large pad of fat, in the region adjoining the prostate.

The left lobe of the *thyroid* appeared somewhat smaller than normal, but of usual consistency and spongy appearance (no section). In the right lobe, the upper portion was of average size, the lower slightly larger than normal, this being due to a mass, about the size of a hazelnut, the surface of which appeared yellow and opaque. On section, this proved to be a definitely encapsulated tumor mass, having a fleshy, pinkish-gray appearance, and in the neighborhood of which there were a number of smaller pulpy, whitish nodules. The histopathological report was adenocarcinoma of the thyroid. The regional lymphatics were somewhat pulpy and red, but only slightly enlarged, and showed no tumor metastasis.

The *spine* was straight, with no evidence of deformity. Upon sawing through the body of the 4th lumbar vertebra, it appeared to be almost entirely replaced by a fleshy, pulpy tumor mass, pinkish-gray in color, with deep red areas here and there. The tumor mass involved the lower portion of the 3d and upper portion of the 5th vertebræ, including the intervertebral discs, and was found to encroach upon the spinal canal, although it did not penetrate the meninges. It proved to be a thyroid adenoma, replacing the atrophic bone, with no evidence of new bone formation.

The 3d lumbar nerve-root, on the left side, appeared to have a small subdural hemorrhage, and later presented a number of unstained fibers. The lumbar and sacral segments of the spinal cord, as well as the nerve-roots of the cauda equina, were submitted to the Kulschitzky-Weigert and Marchi stains. Very slight changes, not conclusively demonstrable, were noted in a few of the lumbar segments, and consisted of only a mild gray degeneration of the marginal zones of Lissauer, some portions of the posterior horns and the columns of Goll on both sides. The lumbar and sacral nerve-roots, except for an occasional faint trace of fat stain, failed to show definite evidences of myelin degeneration. The posterior root ganglia, ventral roots, and the cord tracts, other than those mentioned, remained unaffected.

*Caries of the spine*, as a rule, is associated with more marked curvatures, with less prolonged, less severe, and more symmetrical root irritation phenomena. The finding of other tubercular foci in the body, and



the x-ray examinations will also be important aids in the differential diagnosis. The gibbositities of the spinal column produced by vertebral tumors are less sharp and the pains produced by these tumors are more severe, less symmetrical, more rapidly progressive, and are accompanied by greater cachexia. It would be well to point out here that very often x-ray examinations in cases of spinal cord tumors will show changes in the vertebræ which are interpreted as *spondylitis*. This condition of spondylitis may be, of course, independent of the neoplasm, and bear no relation to it—merely coincidental change in the spine due to the age of the patient, or it may be a reaction of the bone to the pressure exerted by the tumor upon it. A similar condition is found in cases of *brain tumor* where very hyperplastic changes have produced thickening of the bone. This is especially true in cases of long-standing tumors.

Differentiation between *caries* and *tumors* is generally not difficult. Occasionally, however, root pains and the Brown-Séquard syndrome occur in spondylitis. Baettinger has reported a case, which was diagnosed as spinal cord tumor, but which at operation proved to be due to caries associated with abscesses causing compression of the cord. Bruns contends that pain of very long duration does not occur in caries. According to Gowers, the root pains of caries are rarely severe, and are bilateral from the beginning. This is true in many of the cases, but certainly not in all.

Flatau reported a case in which the illness lasted with remissions for almost two years and was accompanied with very severe pain; autopsy showed caries. In these cases the x-ray findings, the presence of temperature, signs of tuberculosis elsewhere in the body, and the von Pirquet test, are of assistance in making the differential diagnosis.

In *gliosis*, as a rule, root symptoms are not present; pain in the back and the radiating pain, while not absolutely always so, are not prominent symptoms in this condition. The vasomotor and trophic symptoms in the skin, soft parts, bones and joints are not as marked in spinal cord tumor as in gliosis, although extramedullary tumors may occasionally give rise to edema.

In typical cases of gliosis, the character and distribution of the anesthesia show the lesion to be in the posterior horn; in extramedullary tumors they indicate that the conductivity of the cord is interfered with. In the former, there is a segmental anesthesia to pain and temperature on the same side; in the latter, in addition to the radicular distribution of the anesthesia, there is anesthesia of the lower half of the opposite side, corresponding to Brown-Séquard paralysis, the anesthesia to pain and temperature being most marked. The symptoms in gliosis extend in a vertical direction, while those of extramedullary tumors extend in a transverse direction. If, after the medullary symptoms have developed, the process goes on slowly and with intermissions, the diagnosis of gliosis is more likely than of tumor. Gliosis is more often accompanied with varying degrees of scoliosis and kyphoscoliosis. When, however, the gliosis is associated with a true glioma, these points in differential diagnosis are not of much value.

*Syringomyelia associated with pachymeningitis* may be mistaken for intravertebral tumors (Oppenheim). In such cases there are root symp-

toms, rigidity of the vertebral column, pain on voluntary motion and on sneezing and coughing, vasomotor and trophic disturbances of the skin, bones and joints, also the segmental type of sensory disturbance with outspoken dissociation, and frequently very marked muscular atrophy. The flaccid paralysis, particularly of the upper extremities, the absence of root phenomena, especially of the posterior roots, all point to the diagnosis of syringomyelia. These symptoms, however, cannot exclude the presence of an intramedullary growth.

*Meningitis serosa spinalis* has been very frequently mistaken for tumor, and the mistake has been discovered only at operation. In these cases a collection of spinal fluid was found which was probably the result of an inflammatory process in the meninges. It is thought by some that the condition bears some relation to tuberculosis, even though tubercle bacilli have not been found. Cases of chronic spinal meningitis have also been described which presented the picture of spinal cord tumor. At operation, scar tissue and a collection of serous fluid have been found. The differential diagnosis between these two pathological meningeal conditions and tumors is, at present, impossible.

*Hypertrophic cervical pachymeningitis* may simulate the early stages of an intravertebral growth. The limitation of the symptoms to those of root or meningeal origin, and the usually favorable course of the disease, will speak in favor of a pachymeningitis.

Multiple tumors, although located on the roots, may occasionally give rise to symptoms of *spinal cord compression* before the appearance of root palsies or disturbances of sensation; in such cases an exact diagnosis before operation is extremely difficult and may be almost impossible. It can be done only by the ability to differentiate between symptoms which occur in one part of the cord from those which occur in another. Occasionally, however, it happens that even though there are multiple tumors, all the clinical phenomena are produced by one growth. The diffuse forms of growth such as *sarcomatosis* and *diffuse gummata* usually present a combination of cerebral and spinal symptoms. At times, especially in sarcomatosis, the compression symptoms are the first to make their appearance; in other cases the spinal cord symptoms develop first. It is interesting, in realization of the difficulty in diagnosis, to call attention to the case which Saenger described and which was examined by Erb, Eisenlauer, and Schultze, and whose diagnosis varied between *tubes*, *syringomyelia*, *neuritis*, and *tumor*.

The greatest difficulty is encountered in the determination whether a neoplasm arises from the cord, or its meninges, or from the vertebral column itself. This can often not be decided until operation. It is important in this connection, however, to remember that most slowly growing benign tumors developing within the neural canal, excepting gliosis, arise from the meninges.

The root symptoms, in tumors arising from the cord substance itself, are not very marked, and the clinical picture resembles that of a *transverse myelitis*, or a *spinal gliosis*. Root symptoms, however, as has been pointed out under Symptomatology, page 339, may be entirely absent even in extramedullary growths. In extramedullary growths the symptoms of root irritation or paralysis do not as a rule ascend, and the upper

limit of the level symptoms remains unchanged or shows a comparatively slight upward extension. As Oppenheim aptly expresses it, "The symptoms show that the tumor becomes thicker, but not longer."

The diagnosis *between extramedullary and intramedullary growths*, especially in the absence of pathognomonic symptoms, is very difficult, and at times impossible. In cases where the differential diagnosis cannot be definitely determined, we are compelled to advise an exploratory laminectomy rather than run the risk of permitting a removable growth to do irreparable damage.

In favor of the diagnosis of intramedullary growths is the slight intensity of the pain, the picture of a subacute or acute myelitis, the ascending type of the medullary phenomena, very marked and frequent remissions in the course of the disease, and in the generally intense character of the symptoms. Quite frequently the clinical picture develops very rapidly in intramedullary growths so that death may occur in a few weeks or months; occasionally, however, the course is a chronic one. Stertz has reported one case which lasted 10 years. Oppenheim reported one lasting 8 years; and the case described by Putnam and Warren appeared to have been 19 years in development. According to Malaise, "Bulbar symptoms appear more frequently in intramedullary than in extramedullary growths. An irregular course, sudden and unexpected changes in the symptoms (probably caused through accessory hemorrhages and inflammatory processes), remissions, absence of the period of pain and tenderness of the vertebral column, and presence of dissociated sensibility or disturbance" are in favor of an intramedullary growth.

*Intramedullary growths* must be differentiated from *multiple sclerosis, spondylitis, tuberculosis, syringomyelia, and meningitis serosa spinalis*. In many cases it is extremely difficult, and at times impossible for a long time, to differentiate these growths from *multiple sclerosis*. In recent years, since we have learned of the many atypical forms of sclerosis, the diagnosis between the two conditions has become even more difficult.

Multiple sclerosis may exist for a long time without causing any symptoms similar to compression; it may also produce the picture of a Brown-Séquard syndrome (Bruns) in certain cases, and cause severe pains. Nonne has observed such cases and ascribed the pains to sclerotic patches. Flatau has observed a case in which the symptoms were entirely spinal, and in which there was very severe pain in one arm and shoulder girdle. He also observed a case in which there was very distinct tenderness of the vertebræ. These symptoms in the beginning caused an error in diagnosis and it was only the later course of the disease which led to the correct diagnosis of disseminated sclerosis. The author has also once observed a case in which there was doubt for a long period as to the differential diagnosis between sclerosis and tumor. Finally an exploratory laminectomy was performed, but no growth was found. The autopsy findings showed a typical case of multiple sclerosis.

Flatau points to the following signs of differentiation between *multiple sclerosis and tumor*:

*First:* The course of illness in multiple sclerosis is not as progressive as in spinal cord tumor. In chronic cases of multiple sclerosis the symptoms do not change essentially in the course of years. Intravertebral tumors, even though they occasionally present remissions, as a rule have a progressive and continuous course.

*Second:* The pain in multiple sclerosis is very rarely severe. Careful interrogation of a patient with multiple sclerosis will frequently reveal the fact that he does not complain as much of pain as of painful paresthesiæ. The pains of sclerosis frequently simulate arthritic pains, and seem to be influenced by changes in the weather. A patient suffering from multiple sclerosis is very unwilling to lie in bed, whereas one suffering from a tumor affecting the meninges has such pain that he prefers to be continually in the recumbent position.

Pain and difficulty during movements of the trunk with considerable local tenderness of the vertebral column on pressure and percussion are marked symptoms in tumors of the spinal column. This pain and tenderness may be absent in meningeal tumors even in advanced stages, but are rarely missing in vertebral tumors. In extradural growths, however, the pain and tenderness may be very prominent symptoms. The writer has rarely seen an extramedullary tumor which did not have tender spinous processes on deep and heavy pressure.

Neoplasms of the spinal column are almost twice as frequent as those of the spinal cord, the nerve-roots, and peripheral roots combined. Malignant tumors are much more frequent than benign. Schlesinger reports the proportion to be thirty to one in a survey of 35,000 autopsies which had been recorded in the "Allgemeines Krankenhaus" in Vienna. In this series he found records of only 59 cases of carcinoma, yet within a period of only twenty-one months he had had occasion to study 10 cases of vertebral carcinoma. Williams reported 16 cases of vertebral involvement in 75 cases of skeletal carcinoma, despite Schlesinger's figures; this would seem to indicate that carcinoma metastasis of the spine must be of much more frequent occurrence. These growths are also metastatic. Skversky has pointed out cases which were formerly considered primary carcinoma of vertebræ, but were really alveolar sarcoma of endothelioma. The primary site of the carcinoma, in order of frequency, is in the mammary glands, the esophagus, the thyroid gland, the uterus, bronchi, stomach, prostate, and gall-bladder.

A spinal cord tumor is differentiated from *transverse myelitis* by the usually acute onset of the latter, without preceding neuralgic pains or root phenomena, and by the history of a preceding infection or infectious disease.

That the diagnosis between *spinal cord tumor* and *chronic myelitis* may sometimes be impossible before operation, is well illustrated by the following case:

CASE X.—A. P. was admitted to the Neurological Service of the Mount Sinai Hospital on November 30, 1917, with the chief complaint of inability to walk. The only significant fact in his past history was that six years before admission he sustained a severe fall and hurt his back. He denied venereal infection by name or symptom.

His present illness began four years ago with slight stiffness and weakness of the left leg. Occasionally he had shooting pains in the same limb, which have lately been getting worse. For the last three months he has had "sticking" pains in the left hypochondrium. Two and a half months ago both legs became paralyzed, and for the last ten days he has been unable to control his bladder.

Examination on admission showed tenderness of the spine between the 12th dorsal and 1st lumbar vertebræ, spastic paralysis of both lower extremities, absent abdominal reflexes, bilateral ankle clonus, bilateral Babinski, exaggerated knee- and Achilles-jerks; anesthesia, analgesia, and loss of temperature-sense below the level of about the 10th dorsal vertebra. A sensory examination three days later showed that the previous sensory changes had extended two segments higher, and there was a distinct zone of hyperesthesia, corresponding anteriorly and posteriorly to the 5th and 6th segments on the left side, and to the 6th and 7th segments on the right side. All abdominal reflexes were absent. Spinal fluid showed 6 cells per cu. mm. Wassermann on the blood and spinal fluid, negative. Diagnosis lay between neoplasm or softening of the cord at the sixth dorsal.

Laminectomy was advised and performed two days later. After the removal of the vertebral arches, there was very active bleeding. The outer surface of the dura was thickened and congested for an area of about 3 cm. in length, in which the cord was densely adherent on the left side. Division of these adhesions caused considerable hemorrhages from the vessels of the cord, which were controlled eventually with cotton pledgets. Probing in all directions disclosed no tumor, and the cord was found to be swollen and flattened. The cord was then covered by Cargile membrane, and the wound was sutured in the usual manner.

Two weeks after operation, examination showed the abdominal reflexes absent; cremasterics absent; right knee-jerk greater than left; in-exhaustible ankle clonus on both sides; double Babinski; a marked "defense" reflex, greater on the right than on the left side, and no changes in the sensory level.

In *hysteria*, while the spine may be fixed with an area of hyperesthesia, it is found that the sphincters are intact, there is no muscular atrophy, the sensory disturbances are peculiar, and the psychic make-up of the patient with sudden onset of symptoms after fright or shock will decide the question.

In 1914, Foster Kennedy and Elsberg described a non-syphilitic inflammatory process of the nerves of the cauda equina, which was followed by an ascending degeneration of the spinal cord. Previous to their publication Oppenheim described a similar case.

The disease usually begins with sharp shooting pains in the back of the legs; the pain is at first unilateral and later extends to the other side. Paresthesias in the involved limbs are regularly present. The progress of the disease is very slow, and it may extend over a period of two or three years. Atrophy of the tibial muscles, with loss of power of dorsiflexion at the ankle, are a prominent feature. The lowest roots of the cauda equina are mainly involved, the sacral roots being affected more severely than the lumbar. The sensory changes, as well as the sphincteric disturbances, depend upon the extent of involvement; the more marked the involvement of the lower sacral roots, the greater the disturbances of the sphincters. The same may be said of the reflexes. At operation a number of the caudal roots are found swollen, congested and of bluish-red color. The cerebrospinal fluid showed no changes in the reported cases, and the dura was not found involved.

The symptoms of this condition are very similar to those of spinal cord tumor, and in many cases a diagnosis cannot be established until exploratory laminectomy is performed.

The following case will illustrate some of the manifestations of this condition:

CASE XI.—J. S., a 19-year-old male, was admitted to Mt. Sinai Hospital on November 24, 1917, with the chief complaint of severe shooting pains in the right lower extremity.

His previous and family history have no bearing on the case. His present illness began fourteen months before with an excruciating, tearing pain, beginning in the right hip and extending down the front of the right thigh and leg. Movement of the limb had no effect on pain. He had occasional paresthesia in the same limb. No other symptoms were present. During the past year he had sought relief from the pain in several hospitals, but without success.

Examination on admission showed the patient rolling around the bed with the right thigh and leg flexed, apparently in agonizing pain. There was no limitation of motion and no pain on active or passive motion of both hips, knees or ankles. Right knee-jerk was less active than left. Achilles-jerks could not be elicited on either side. No Babinski.

The cerebrospinal fluid was under normal pressure, and contained 49 cells, 34 being lymphocytes. Wassermann negative on blood and spinal fluid.

A reëxamination two days later showed, in addition to the findings on original examination, some hypotonia of the right leg and a definite atrophy with slight iliopsoas spasm of the left leg. Right abdominal reflex diminished; right gluteal reflex diminished; all forms of sensation were diminished in the lower part of the right leg. Fundi normal.

Nov. 28, 1917. Received 0.25 gram arsenobenzol intravenously, and on Dec. 3, 1917, it was noted that there was a perianal hypalgesia which extended along the sacral distribution of the posterior aspect of the right thigh. On December 4th, he received 0.3 arsenobenzol intravenously, and a similar dose on December 6th and 8th. On December 8th, both knee-jerks were found to be livelier and at times the left Achilles was obtainable.

In spite of the antiluetic treatment, the patient showed no signs of improvement. His pains persisted and there was no change in sensation, or in the partial atrophy of the right leg.

December 12th. Lumbar puncture yielded a spinal fluid with 34 lymphocytes. Wassermann on spinal fluid and blood, negative.

The diagnosis of tumor in the lower lumbar and upper sacral regions was then made and a laminectomy advised. At operation, no tumor or adhesions were found, but Dr. Elsberg, who operated on the patient, found the nerves of the cauda were pink instead of gray, and made the diagnosis of neuritis of the cauda equina.

Four weeks after operation, examination showed slight atrophy of the right thigh and right leg; marked weakness in right lower extremity; left knee-jerk somewhat diminished; right knee-jerk present but weak; both Achilles-jerks absent; extension of right leg accompanied with great pain; slight tenderness on pressure over the entire lumbar and sacral regions of the vertebral column. Patient unable to sit or stand.

*Sensory Changes:* Right leg, anteriorly.—Very definite zone of hypesthesia in the distribution of the 5th lumbar and 1st sacral; marked hypalgesia in the distribution of the 1st sacral; thermal sense slightly affected, if at all.

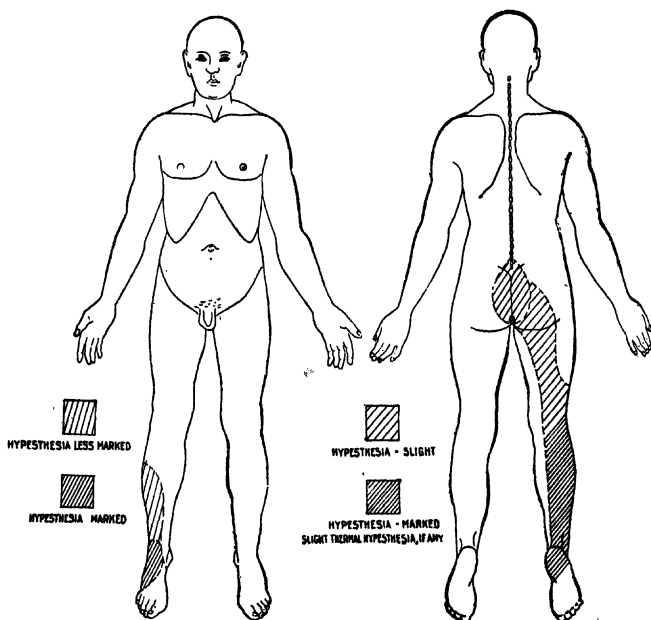


FIG. 8.—CHART OF SENSORY DISTURBANCES IN CASE XI. (J. S.)

Posteriorly.—Slight hypesthesia in the area of the distribution of the 4th, 5th and 3d sacrals, more marked hypesthesia in the distribution of the 1st sacral and 5th lumbar; slight thermal change, if any. Deep muscle sense in that leg apparently lost.

Two weeks later, examination showed right thigh and right leg atrophied; motor power considerably diminished; seems to be able to raise the leg but with great difficulty; great tenderness on pressure on back

of leg; right knee-jerk can be elicited at rare intervals; sensory disturbances present in the same distribution but not as marked; both Achilles-jerks absent; cremasterics sluggish.

One month later the patient began to walk around the wards of the Hospital, and although he dragged the right foot and complained occasionally of pain in it, he appeared to be quite comfortable. Before his discharge from the Hospital (five months after admission) examination showed the upper part of body uninvolved. Both knee-jerks present, but left greater than right; Achilles-jerks elicited occasionally, and even then with difficulty; considerable wasting of the right thigh and leg; and no marked difference in the sensory changes from the last examination (*see* above). Lumbar puncture yielded fluid which was negative as to the Wassermann reaction, and contained 14 cells to the cu. mm.

At this writing, the patient is an orderly in the wards of Montefiore Home and Hospital. He is up and about attending regularly to his work. He does not complain of pain except before the onset of rainy weather, and then his pain is relieved by aspirin, and even then, i.e., while taking the aspirin, he is not incapacitated from doing the hardest physical labor. Upon examination no material change is found in his motor or sensory manifestations since the last status which was made at the time of his discharge from Mt. Sinai Hospital.

As far as the diagnosis of localization of tumors of the cord, the following points, in addition to those discussed under Symptomatology, are to be borne in mind:

A patient with a spinal tumor may complain of various pains in the back, or may have paresthesia due to irritation of the long sensory spinal cord tracts, or girdle pains, but these are not constant and not as persistent as the root pains; the latter, therefore, are the pains to be considered in the localization of new-growths. A zone of hyperesthesia above the anesthetic area is an important point in determining the level of the lesion. When a segmental area shows a well-marked anesthesia, it may be concluded that at least one segment above that by which the area is innervated is, in all probability, severely damaged. The highest indication of any disturbance of function is the safest guide. It is due to the neglect of this fact that tumors of the cord are often looked for at too low a level, and are not found until one or two more laminæ are subsequently removed. It is wise, therefore, that laminectomy be performed 8 to 10 cm. above the upper limit of the zone of anesthesia. The downward extent of the lesion is generally impossible to determine.

A study of the loss of the root or spinal reflexes, which are usually absent in the corresponding area owing to compression of the roots and of the cord itself, is also a great diagnostic aid. Degenerative paralysis as a root symptom, whether due to compression of the roots or of their segments of origin, is also of great importance as a diagnostic symptom, especially in tumors of the cervical, lowest thoracic, and lumbar sacral cord.

Tenderness on pressure of one or more vertebræ, with roentgenological studies of the spine, will, in conjunction with the other symptoms,



especially the development and extension of the various root and cord symptoms, be helpful aids in the determination of localization.

In primary intravertebral tumors, prior to laminectomy, it is impossible to venture a diagnosis as to the nature of the neoplasm, and for practical purposes, this makes no difference, because the same treatment—laminectomy—is indicated, no matter what the histological character of the neoplasm may be. In tumors of the vertebræ, whether primary or secondary, it may be much easier to determine the exact nature of the growth, but in most of the cases, as Buzzard says, "the knowledge thus acquired unfortunately contra-indicates the hope of a radical cure."

It is well to bear in mind, however, that in many instances the question of diagnosis can be positively answered only after an exploratory laminectomy, and it is therefore most advisable to give the patient the benefit of the doubt in any doubtful case and resort to an early exploratory laminectomy.

DIAGNOSIS ON LABORATORY FINDINGS.—*Spinal Fluid*.—Lumbar puncture is indicated in every case where there is a suspicion of a spinal cord neoplasm. Examination of the spinal fluid is important because, in the first place, it may point to the presence of syphilis, and secondly, because the character of the fluid may be altered in a fashion which is characteristic of spinal cord compression. The change in fluid is spoken of as the Nonne-Froin reaction, or the xanthochrome reaction.

The fluid is of a deep lemon-yellow color. The globulin is markedly increased, the cells are very often increased in number, and are principally lymphocytes.

Very often the fluid clots spontaneously a few minutes after it has been withdrawn. The color of the fluid and the increase in globulin may be the only indication of this reaction. The clotting and the increase in cells may be absent. Extradural abscesses and pachymeningitis suppurativa, by the compression of the cord, may also give this reaction in the spinal fluid. These two conditions, however, are rare, and generally the other symptoms are such that a spinal cord neoplasm can be excluded. The author has never seen this reaction in a case of syphilis of the membranes or of the cord.

With the above named exceptions, the xanthochrome reaction may be considered pathognomonic of spinal cord compression from neoplasm, hence it is a symptom of the utmost importance in diagnosing such growths. Frazier is incorrect when he states that this reaction may occur in infectious diseases. He does not ascribe to it the importance which it should have in the diagnosis of spinal cord tumors.

The lemon-yellow color alone and the increased cell content may be found after cerebral hemorrhage and occasionally even in cases of neoplasm in the brain. This fact, however, is not of moment in the consideration of spinal cord neoplasms. The coloring agent is thought by some to be due to hemosiderin, but other investigators have not been able to confirm this finding, so that at present it may be stated that the nature of the pigment is unknown.

A lumbar puncture at times results in a remission of the symptoms produced by the neoplasm. This remission, however, does not affect the important diagnostic symptoms, and should not lead one astray in the diagnosis.

**Treatment.**—Prior to 1887, patients suffering with spinal cord tumors were doomed. A ray of hope began to shine for these unfortunate sufferers when Erb, in 1878, raised the question of the advisability of operating on spinal cord tumors, and when Secat, Gerster, and other pioneers in this direction actually began to remove tumors growing outward, or those pressing from the outside towards the spinal canal. These operations were of inestimable benefit to humanity, not only because they relieved the sufferers from spinal cord tumors, but because during the operations conditions were met with which cast light on many obscure features in the physiology and pathology of the cord and its tracts, thus enabling more definite localization, and therefore more accurate diagnosis.

The epoch-making operation was not performed until 1887, when Horsley removed an extramedullary almond-shaped tumor from the upper dorsal cord of the left side, from one of Gowers' patients, a man of 42, who three years before began to suffer with severe left-sided intercostal pain. During these three years his pain could on several occasions be controlled and the condition was considered to be one of intercostal neuralgia; when, however, the left leg began to show signs of paralysis, which gradually extended to the right leg and was accompanied by exaggerated reflexes, spasticity and sphincteric paralysis, the diagnosis of spinal cord tumor was made and an operation was decided upon, which when performed showed that the tumor had been localized correctly, and was removed. The patient made an uneventful recovery. It was this operation which put neurologic surgery, as far as disease of the spinal cord is concerned, on a definite scientific basis.

Gowers and Horsley gave it as their opinion that intradural tumors, owing to their slow growth and loose connection with the cord, were benign and therefore almost always operable. Schlesinger, from a study of his autopsy material, was not as optimistic in this respect, but subsequent results have practically justified Gowers' and Horsley's conclusions.

The actual technic of operations on the spinal cord tumors is not within the scope of this chapter. There are, however, some points which the physician, upon whom the responsibility of diagnosing a spinal cord tumor rests, must bear in mind in order to be able to coöperate intelligently with the neurologic surgeon in the treatment of the case.

In general, it may be said that a larger number of tumors of the cord, being more easily localizable and more accessible to operation than brain tumors, offer better prospects for the relief of symptoms and eventually permanent recovery after surgical interference than the latter.

Solitary extramedullary tumors are amenable to **surgical treatment**, provided the level diagnosis can be established with some reasonable degree of certainty, but the same cannot be said of multiple or diffuse tumors. The most favorable tumors for operation are those which are small in size, solid in consistence, sharply limited and benign in nature, arising

from the membranes and displacing the cord; those lying on the anterior surface of the cord are more difficult, but not impossible, to remove. Tumors may be removed from any level of the cord, but those which are localized in the dorsal region offer the best results; they are being removed successfully from the highest cervical region as well as from the cauda equina, but the postoperative mortality in the latter region is considerably higher than at other levels. Söderbergh and Akerblom removed successfully an endothelioma pressing on the cervical segments, and Frazier removed a similar tumor with success at the level of the 3d cervical vertebrae in a patient sixty-four years of age.

In any case, *the earlier the operation* the better the outlook for recovery of function. The ideal time to perform any operation upon these growths is before the disease has passed the second phase—the phase of Brown-Séquard paralysis. The duration of several years, however, does not necessarily imply futility of operation, provided the symptoms of compression have not been of too long standing. A patient, who is exhausted by long suffering, addicted to narcotics, and afflicted with a bed-sore, or an ascending pyelitis from an infected bladder, can certainly not be considered a good surgical risk.

There are always a certain number of cases in which a positive diagnosis as to the presence of a growth, its nature, or its exact localization cannot be made. In such instances an **early exploratory laminectomy** is indicated. Whenever there are indications of a new-growth or of a chronic inflammatory lesion, and the patient's general condition is such that any operative procedure is not contra-indicated, an exploratory laminectomy is to be resorted to; such an exploration in the hands of an experienced neurologic surgeon is devoid of danger and may, in selected cases, even be performed under local anesthesia. When the clinical history of the case and the serological findings of the blood and spinal fluid indicate the possibility of a luetic lesion, **energetic antisyphilitic treatment** is indicated, but if within a month after such treatment has been instituted the patient shows no marked improvement, operation should not be delayed.

Exploratory laminectomy is indicated whether the tumor is suspected of being in the highest or lowest part of the cord. While the extramedullary tumors are more favorable for surgical intervention, a suspicion of the presence of an intramedullary tumor is no contra-indication to an exploratory laminectomy.

Over a decade ago, Bruns announced that the **removal of intramedullary tumors** was impossible, but in 1907 Eiselsberg removed one such tumor successfully, and since then Frazier collected 36 cases from the literature which were operated on with a complete cure in a few cases, and the return of function in a larger number.

The technical difficulties encountered in the removal of a growth in the cauda equina do not make operations in this region as promising in ultimate results as operations in other parts of the cord; but even here, when without operation the mortality is 100 per cent., operation should

be undertaken. Naturally operations in this region require painstaking after-care, because most of these patients have been suffering from incontinence of urine and feces before they reach the operating table, and are therefore in constant danger of infecting the wound of the laminectomy.

All operations on cord tumors should preferably be *one stage operations*, except in circumscribed intramedullary tumors, in which the experience of some has shown that, owing to the danger of mutilating the cord during total enucleation of the growth at the first operation, it is better practice to expose the growth and leave room, so to speak, for the tumor to extrude itself.

An incision into the posterior longitudinal septum of the cord, which is carried down to the tumor and even the sacrifice of the posterior longitudinal columns of the cord, do not cause any important functional disturbance, and therefore this does not need to deter the operator from performing a complete operation.

While the removal of three laminae is the established minimum, no matter how many laminae are removed, the stability of the spine does not seem to be impaired except possibly in the cervical region. The writer has seen as many as seven laminae removed without the patient suffering any inconvenience and without any resulting deformity of the spine.

Bilateral laminectomy is preferable to unilateral laminectomy, because, the exposure being wider, exploration is easier and the cord can be manipulated with greater impunity and with less chance of injuring it. Laminectomy should be begun so that the lowest segments or corresponding root represented in the upper limit of the zone of anesthesia is the guide, and the operation continued upward. If the roots are involved with the growth, these may be resected with the growth without harm; the resection of one, two or three posterior roots at any level is not as serious a matter as the resection of as many anterior roots, particularly when these supply the upper or lower limbs. A resection of anterior roots in this distribution will permanently interfere with motion of the involved limbs, but this fact will also have to be disregarded if the roots are incorporated in the growth. In the case of tumors of the cervical and lumbar regions, lying on the anterior surface of the cord, it may be necessary to sacrifice one or more of the posterior roots in order to remove the tumor.

When the diagnosis of an extradural tumor is made and no tumor is found, the dura must be opened and search made for an intradural growth. In fact, failure to find a tumor at the expected level should always be followed by a search up and down the cord for a number of segments. This search is preferably made by inspection rather than probing.

The majority of primary tumors of the vertebræ are benign, hence they are generally operable. Those originating from the arches are easily removed, but those originating from the bodies themselves are beyond surgical aid. Secondary tumors being as a rule malignant—metastatic in nature—interference is contra-indicated, and is at best palliative in nature. When the agonizing pain becomes unendurable, posterior

**rhizotomy or section of the anterolateral column of the cord** should be performed; mere decompression in such cases is of little or no value.

It is not unusual for the paralysis to become aggravated immediately after the operation, and therefore no prognosis as to the final outcome should be based on the amount of paralysis or sensory disturbance present within a few days or weeks after any operative procedure on the cord. Occasionally a transverse myelitis follows the removal of a tumor, and the patient remains paraplegic or dies. The cause of this unfortunate complication is not known. When the spastic paralysis has not become flaccid, and the reflexes not entirely abolished after operation, the outlook for a favorable result is good. The final outcome in all cases depends upon the amount of compression that the cord has been subjected to prior to the operation. *After operation*, the judicious employment of well-directed **gymnastic exercises**, with **electricity and massage**, will aid in the restoration of function.

Tumors in which surgical intervention is out of the question may occasionally be favorably influenced by **radium, x-ray or Coley's fluid**. There are cases in the literature in which these procedures cured the patients; radium and x-ray seem to be more beneficial in sarcoma than carcinoma. The treatment by "**extension**" is absolutely contra-indicated, because this aggravates the patient's condition without having the slightest beneficial influence on the neoplasm. In fact, in cases in which the diagnosis is between Pott's disease and spinal cord tumor, the application of "**extension**" may be of diagnostic aid, because, while in Pott's disease the patient's symptoms will be at once relieved, they will be considerably intensified in cases of tumors.

**Course, Duration, and Prognosis.**—These depend upon whether the tumor is benign or malignant, whether single or multiple, its situation, how early the diagnosis is made, how soon operation is resorted to, with what ease the tumor can be removed, and what liability exists as to its recurrence, or metastasis.

As a general rule, the onset is gradual and the development slow. Occasionally the symptoms may appear suddenly. The following case of spinal cord tumor is a good illustration of a sudden onset:

**CASE XII.**—A. R., female, 22 years old, was admitted to Mt. Sinai Hospital on May 16, 1913, with a family, personal and past history which had no bearing on the case. Her present illness began suddenly three months before admission, when without any previous pain or disability she collapsed while walking. When she was picked up she was unable to walk, owing to weakness of the right leg. Immediately thereafter she noticed that the affected limb became spastic; her urination was frequent, every half to one hour day and night; and she became markedly constipated. She had no pains, no paresthesia, no twitchings, no headache, no dizziness or vomiting. During the three months prior to her admission to the hospital, there had occurred no wasting of any muscle of the body.

Examination on admission gave the following positive findings:

Moderate enlargement of both lateral thyroid lobes; absence of all abdominal reflexes; both lower extremities spastic, more marked on the right; both knee-jerks, exaggerated; bilateral Babinski and bilateral ankle clonus. Loss of sensation up to nipple line, for pain and temperature on both sides, but less marked on the left side. On May 17th, the examination of the fundi showed them to be normal. On May 18th, lumbar puncture yielded 6 c.c. clear greenish-yellow fluid under decreased pressure; cytology normal. On May 22d, she began to complain of pain in the right shoulder, and a sensory examination elicited that the above-mentioned sensory changes were ascending higher. The Wassermann reaction of the blood serum and cerebrospinal fluid was negative. The roentgenologist reported "irregularity of the bodies of the 3d, 4th and 5th cervical vertebræ." Upon these findings, a diagnosis of intramedullary tumor of the lower cervical and dorsal cord was made and laminectomy advised. At the operation, which was performed four days later by Dr. Elsberg, a typical glioma 6 cm. long was found beneath the pia, between the 5th cervical and 3d dorsal. The operation was a two-stage one, and 11 days after the laminectomy, the tumor was extirpated. Two weeks after this, an examination showed a slight wasting and weakness of the right lower extremity; right arm and forearm weak. Knee-jerks, exaggerated; bilateral Babinski and bilateral non-exhaustible ankle clonus. Three weeks later the power of the legs began to return and the patient was able to stand by herself. By this time her urinary and bowel disturbances had entirely disappeared. One week later, the spasticity of the legs had almost entirely disappeared, and the patient could stand and walk a few steps without assistance. When she was discharged from the hospital on July 24, 1913, she could stand and walk. Her knee-jerks were but slightly exaggerated. There were still a bilateral Babinski and Oppenheim, and a bilateral exhaustible patellar and ankle clonus. The upper abdominals were present but weak; the lower were not obtainable, and there was diminished tactile and pain-perception in both lower extremities.

In some cases symptoms of root irritation may be present for years before the symptoms of compression of the cord make their appearance. In one of Schultze's cases, the growth was benign and death occurred four months after the onset of the first symptoms.

Periods of remission and exacerbations which may lead to errors and doubts in diagnosis are not very usual but, as with new-growths in other parts of the body, are by no means very rare.

The duration of spinal tumors, from the onset of the first symptoms to the time of operation or death, may vary anywhere from fifteen days to fifteen, twenty, or even twenty-five years. Isolated nodules of sarcoma, fibroma, or psammoma may exist for years without producing any symptoms whatever. Tumors of the cauda equina are of comparatively longer duration, because they have more space in which to expand, but tumors in the lumbar and thoracic regions, for reasons unknown, appear to grow more rapidly.

In the cases of vertebral tumors, whether they be carcinomatous or sarcomatous, an unfavorable outcome may usually be expected anywhere from nine months to a year. In intravertebral growths life may be prolonged for two or more years. In the cases of sudden paraplegia, following collapse of tuberculous or carcinomatous disease of the spinal column,

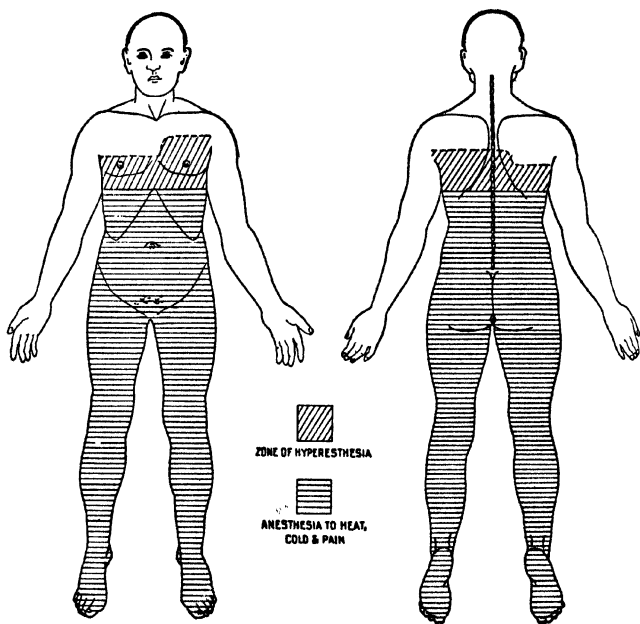


FIG. 9.—CHART OF SENSORY DISTURBANCES IN CASE XII. (A. R.)

resulting in a myelitic process of the cord, the duration may be unusually short. The duration of the disease, as has been said before, depends on whether the tumor is amenable to surgical treatment or not, and is also influenced by the presence of bed-sores, cystitis, ascending renal involvement and complications in other vital organs.

Recovery without surgery cannot be looked for, except perhaps in syphiloma. Parasitic growths and cysts may be arrested by calcification, but such a fortunate outcome is unusually rare. Henschen has seen a case which he could attribute to the regression of a neuroma, and Oppenheim knew of a case in which, after an operation had been decided upon, the patient had developed some intercurrent febrile disease, after which the symptoms of tumor improved to a considerable extent.

The prognosis is most favorable in cases of localized benign tumors in

the extradural or intradural spaces, and least favorable in the diffuse or multiple extramedullary tumors and in all of the intramedullary ones.

The degree of recovery depends upon the amount of damage inflicted on the cord before operation. If the degeneration has advanced too far, even if the growth is localized, benign and completely enucleated, restoration of function cannot be expected. Fortunately the compression of the cord may be severe and prolonged, without destroying all hope that its functional activity can be restored if the pressure is removed. Before operation, it is impossible to foretell how much restoration of function can be looked for, and it is impossible to state whether the loss of function is due to compression by the tumor per se, or to a myelitis as a result of pressure.

Restoration of function in most cases does not occur immediately after operation; as a rule it does not take place until six months later, and may not occur even for two years after the removal of the tumor. The author has seen a case in which, after the removal of an intramedullary tumor in the lower cervical and upper dorsal regions, it took three years after the operation before evidences of restoration of function began to make their appearance, and it took three more years after this before restoration was complete. Restitution of function after removal of tumors may, however, be remarkably prompt even if the cord has been flattened out. Pain and sphincteric disturbances usually disappear rapidly.

The sensory disturbances are relieved sooner than the motor; the impairment of pressure-sense (bathyanesthesia) is most persistent; impaired muscle power is regained first in the muscles which became last involved in the process. The diminution and final loss of spasticity also depends on the degree of degeneration of the pyramidal tract, and if this has been considerable, it may never disappear.

The earlier the diagnosis is made and the sooner operation is performed, the more favorable the prognosis both as to life and restoration of function. The possibility of the existence of a spinal tumor must always be borne in mind whenever a case presents motor or sensory symptoms whose origin cannot be definitely determined, and as has been pointed out under Treatment, exploratory laminectomy is in all such cases a perfectly justifiable procedure.

Generally speaking, tumors in the thoracic region offer a better prognosis after proper surgical intervention than tumors in the cervical, lumbar, or cauda equina regions. The most favorable cases are those in which tumors arise from the meninges, and least favorable when they arise from the vertebræ. In patients under twenty years of age, the prognosis is, comparatively speaking, better than in older patients. The nature of the growth has a very important bearing on the prognosis. It is best in benign growths, next best in endothelioma, and worst in cancer and glioma. The patient's general condition prior to operation, emaciation, decubitus, cystitis, etc., even if the tumor is found to be easily removable, makes the prognosis very doubtful.

**Pathology.**—**EXTRAMEDULLARY TUMORS.**—Extramedullary tumors are more common than intramedullary ones; they develop very slowly,



the symptoms at first being due to their compressing the cord laterally. As a result of such compression the cord may be reduced very markedly in its size, or flattened to a considerable degree. In spite of the degree of pressure which these tumors may exert, it is found that, owing to their gradual development, the degeneration of the cord elements is not as marked as one would expect, and after removal of the tumor, the cord readily reassumes its original contour and function. It seems that, unless the pressure exerted is extreme and has persisted for a very long time, complete destruction of the cord does not occur.

The *vertebræ*, especially their bodies and less commonly their arches and processes, are frequently the site of neoplasms, which may be malignant or benign. The malignant growths include carcinoma, sarcoma and myeloma. Carcinoma of the *vertebræ* is usually secondary, generally metastatic from the heart, stomach, intestines, esophagus, lungs, kidney, thyroid, uterus or prostate, etc. The lumbar and thoracic portions of the column are more often involved than the cervical or sacral; the involvement may be limited to one or more foci or may extend to many *vertebræ*. The growth may attack first the spongy portions of the bones destroying the medulla, the compact bony cortex forming for a time a "shell" around the neoplasm. This osteoplastic process may be so extensive that a firm ankylosis of a portion of the spinal column may ensue, producing apparently no deformity. More commonly, however, the softening produced by the infiltration of the bones allows the body weight to cause a general shortening of the spinal column, or it may lead in localized areas to a variety of carcinomatous caries not unlike that of tuberculosis, producing a typical Pott's disease deformity. When the latter occurs, the nerve-roots near or within the intervertebral foramina become compressed; occasionally carcinomatous nodules from the inner surface of the vertebral bodies or their arches may project into the neural canal and compress the spinal cord itself.

Sarcoma of the spinal column may be primary or secondary, or it may be circumscribed or multiple and diffuse. The lumbar and sacral regions seem to be the most favorite sites for this variety of growth. The mechanical effects on the vertebral column may be the same as has been described in carcinoma. The secondary sarcomata may extend directly from the neighboring tissues or they may be in the form of metastases from more remote parts of the body. Metastatic sarcoma of the *vertebræ* is not as common as metastatic carcinoma; according to Schlesinger, secondary sarcoma of the spinal column is most common when the primary sarcoma is of bony origin. Sarcomata of the *vertebræ* grow very rapidly and involve the roots early.

Myeloma of the vertebral column is less common than carcinoma and sarcoma, and less common than the benign bony and cartilaginous growths. Multiple myeloma may render large portions of the column soft and result in deformities with consequent compression of the cord and the nerve-roots. Single myeloma is quite rare. The ribs, sternum, and bones usually participate in the general myelomatous involvement. While myelomata are generally soft and pliable, ivory-like ossification

of some of them is occasionally encountered. Myeloma seems to affect males more commonly than females.

Benign tumors of the spinal column are rare and include osteomata and exostoses, chondromata and osteochondromata, myxomata, callosities, and the osseous changes encountered in arthritis deformans. Osteomata develop gradually and are rarely of sufficient size to cause compression of the cord. There are, however, in the literature reports of unusually large osteomata. All of these are of neurological interest only when they extend into the neural canal, and by compressing the cord and its roots, produce motor or sensory symptoms, or both.

Spinal caries (spondylitis tuberculosa) usually begins in the bodies of the vertebræ, less commonly in their joints and ligaments, and still less commonly in their arches and processes. Tuberculosis of the body of a vertebra begins usually as a localized soft spongy granulation which leads to a softening of the osseous tissue and finally results in caseous or purulent material. This may occur in one or several adjacent vertebræ, but very rarely, if ever, in several vertebræ *remote* from one another. If the process advances to the stage of necrosis of one or several vertebral bodies, the neighboring vertebræ collapse, causing a marked deformity. The danger to the cord and its adnexa is both from compression resulting from the displacement of the vertebræ and from the soft, cheesy, purulent, tuberculous material invading the neural canal. While such compression is, as a rule, gradual in its development, a sudden giving way of the diseased vertebral column may lead to an immediate dislocation giving rise to a sudden onset of symptoms of compression of the cord and its roots.

Acute osteomyelitis of the vertebræ is rare. We have seen one such case.

Spondylitis typhosa, which is an inflammatory condition of the spine occurring during or after typhoid fever, is not uncommon.

Martens has seen actinomycosis of the spine following an extension of the disease from the lungs.

Simple traumatic spondylitis may also occur, and by extension into the neural canal may give rise to symptoms of nerve-root irritation.

Occasionally syphilis of the vertebral column is encountered in the form of exostoses on the bodies and transverse processes, which compress the cord and the nerve-roots. When gummata do occur, they are found to arise either in the substance or on the surface of the bone. A syphilitic form of spinal arthritis has also been described by several authors. On the whole, however, while syphilis is very common in such bones as the tibia, clavicle, and the skull, it is comparatively rare in the vertebræ. Nonne has emphasized that syphilitic growths practically never involve the cord. Gummata, when they are found, are most commonly extramedullary—very rarely intramedullary. They do not yield to antiluetic treatment, but must be treated surgically in the same way as other tumors.

Excluding tumors of the vertebræ, extramedullary tumors situated *outside the dura* are much rarer than intradural tumors. Primary growths are very rare. Fibromata and fibro-endothelioma which may

become psammoma, fibrosarcoma and melanosarcoma, and chromatophoroma are the most common. These tumors may be intradural or extradural. Primary sarcoma of the meninges usually originates from the inner surface of the dura. Some of the cases reported in literature as true sarcomata have undoubtedly been endotheliomata. Occasionally lipomata occur in the caudal region. Teratomata containing cartilage and fat tissue have been found in the sacral and coccygeal regions. Secondary tumors are much more frequent. They are found usually on the outer or inner surface of the dura and grow into the dura from without. Tumors of the spine especially have a tendency to grow through the dura.

Occasionally lymphoma, as in Hodgkin's disease, may infiltrate through the intervertebral spaces and may even grow through the dura within the dural sac, or it may present a typical appearance of a tumor formation, and thus produce compression of the cord and the nerve-roots. The following case of extradural lymphoma, giving typical symptoms of a spinal cord tumor, came recently under our observation:

CASE XIII.—R. W., female, 25 years old, was admitted to the Mt. Sinai Hospital on July 26, 1916, with the history that she had been a patient in the institution ten months ago, and was discharged as "temporarily relieved," with the diagnosis of Hodgkin's disease. During these ten months she had been quite comfortable, until two weeks ago when she began to have pain in the right shoulder; the pain was constant and radiated to the front of the chest and to the breast; it was increased by raising the arms. One week later, the left side of the chest also became painful, and she began to have paresthesia and stiffness in the right leg. At the same time she noticed that the leg was weak and a day or so later this leg became totally paralyzed; two days before admission the left leg also became paralyzed. Urinary and sphincteric disturbances set in three days before the paraplegia had become complete. She also had a sense of constriction over the entire body from the costal margin down.

Examination showed the left pupil larger than the right (this followed the removal of a gland from the left side of the neck for diagnostic purposes during her last stay in the hospital); slight rigidity of the neck; a herpes zoster on the breast and axilla in the distribution of the 3d, 4th and 5th dorsal nerves. Vibration sense was lost up to costal margin, and complete motor paraplegia. Both triceps reflexes, sluggish; wrist-jerks, not elicitable; all abdominal reflexes absent; knee- and ankle-jerks, active; left plantar reflex, more lively than the right. Tenderness was felt on pressure over 2d and 3d dorsal vertebræ. Fundi, normal. Upon these findings a diagnosis of compression of the cord between the 2d and 3d dorsal, probably a lymphoma, was made. On July 27, 1916, laminectomy was performed and an extradural tumor the size of a hickory nut between the 2d and 4th dorsal vertebræ was found and removed. The tumor, on examination, proved to be a lymphoma.

INTRAMEDULLARY TUMORS.—*Primary Growths of the Pia Mater.*—The most common growths of this membrane are the fibroma (uncommon),

myxoma (very rare), and sarcoma, especially round-celled ones. According to Schlesinger, primary sarcoma of the meninges shows no tendency to metastasis, and in most cases does not involve the spinal cord. While primary sarcoma of the cord itself is very rare, it may occasionally infiltrate the meninges of the entire cord and give rise to the interesting condition spoken of as "sarcomatosis of the cord." In these cases the growth also extends upward to the base of the brain and infiltrates the cord along vessels and the septa. Sometimes, in addition to this diffuse sarcomatosis, isolated sarcomata may be found in different areas of the central nervous system. The structures in the posterior fossa of the skull, especially the cerebellum, are generally involved in these cases of multiple sarcomata. As a general rule, spinal sarcomata are not as malignant as sarcomata in other parts of the body, but after they have invaded the meninges, their removal becomes impossible. Diffuse gliomatous infiltration of the meninges has been described, but it is extremely rare. Occasionally the involvement of the meninges both by sarcoma and carcinoma may be so minute that they can be discovered only microscopically. The endotheliomata are fortunately fairly common tumors in the meninges. They are usually diagnosed as endothelioma or classified as fibro-endothelioma or fibrosarcoma. They are, as a rule, solitary and yield easily to complete extirpation.

Occasionally rarer forms are encountered such as angiosarcoma, cylindroma and endothelioma, which probably arise from the endothelium of the arachnoid. Fibro-endothelioma and epithelioma, occasionally melanotic sarcoma metastases may be found; the latter form small deposits which are widely scattered over the dura. In the caudal region, lipoma and myolipoma occur. Both of these occur frequently in combination with spina bifida. Multiple neurofibroma, which may grow to almost the size of a walnut, occurs rather frequently along the nerve-roots and may be part of general neurofibromatosis.

*Secondary Growths.*—Carcinoma and sarcoma, and glioma of the retina which follows the sheath of optic nerve along the base of the brain may grow down along the cord.

The tubercle, glioma, and sarcoma are the most frequent forms of intramedullary growths. Primary intramedullary sarcoma without involvement of the meninges is very rare. Schlesinger found in his material 13 such cases. In some cases, the sarcoma involves a considerable area of spinal cord, the tumor mass being sharply encapsulated. Church and Eisendrath were unable in one case to enucleate such a growth from the region of the posterior longitudinal septum.

Among the rare kinds of growth are angioma, neuro-epithelioma, gliomatous microcysticum, neuroma, cholesteatoma, chromatophoroma, endothelioma, teratoma, cysticercus, and carcinoma metastases. Schlesinger's report on spinal cord tumors mentions the tubercle as the most frequent form. There may be numerous miliary tubercles surrounded by areas of softening, or a solitary conglomerate tubercle. The tubercle may arise either in the gray or white matter of the cord, and may be so small that the contour of the cord is not altered, and thus may be over-

looked at operation. The glioma is the next most common form of growth. It is rarely solitary but extends for some distance up and down the cord. It may grow along the entire length of the cord and extend even into the medulla; it generally occupies the center of the cord, or lies just to one side of it. The glioma remains in the cord, but the gliosarcoma infiltrates the dura. Gliomata proper never originate in the meninges; they are very vascular and may grow out into the nerve-roots. Occasionally glioma is combined with syringomyelia. Glioma has also been described in association with neurofibroma and angioma.

Intramedullary gummata occur very rarely.

Involvement of the spinal cord is comparatively uncommon in all forms of leukemia. The most common lesions found are hemorrhages, which are encountered more frequently in the brain than in the cord; degeneration of the cord similar to those met with in pernicious anemia and other toxic or infectious conditions; small foci of leukemic infiltration of the cord substance, combined with hemorrhage, necrosis and macroscopic epidural or dural infiltration, which may be sufficiently large to produce symptoms of compression of the cord.

Peter Bassoe reports the following case of a woman of 28 years who had been suffering from splenomedullary leukemia for over three years:

CASE XIV.—After a considerable period of remission from her symptoms, she was suddenly seized with severe pain in the chest, which was followed the next day by a complete paraplegia and urinary retention. At this time the leukocyte count was 286,000 and 51 per cent. myelocytes. The spinal fluid showed no increase in cells but increased globulin, and a positive Lange colloidal-gold test with a reaction mainly in the higher dilutions. Death occurred five weeks after the onset of the paraplegia. At autopsy, there was found a tumor-like myeloid infiltration of the spinal column extending into the neural canal, and forming a tumor-like mass 12 cm. long, along the dorsal region of the spinal cord. The cord itself in this region was necrotic and deformed from compression, but showed no infiltration nor was there any evidence of a preëxisting degeneration.

Cysticercus occurs occasionally within the dural sac. Echinococcus develops either within the dural sac or on its outer surface. These are generally not primary, but arise from the muscles of the vertebral column or from the subpleural or retroperitoneal tissue. Very rarely do they grow out of the vertebral column itself.

Parasitic cysts within the vertebral canal are either cysticerci or echinococcus cysts; the latter are about five times more frequent than the former. Cysticerci are more likely to be overlooked, because in any one case, they may be smaller and less numerous, and are never found within the vertebral canal unless they exist elsewhere in the body, especially in the brain and its membranes; they are round or oval, and rarely do they show processes. They are much more common intradurally than extradurally. From one to seven cysts have been found in the vertebral canal.

They are frequently found on the ventral side of the cord, sometimes within its substance, and are usually the size of a pea. They may be free or they may be attached to the spinal cord. When an echinococcus cyst is intradural, it is round or oval, and compresses the cord. The dura is usually not implicated; it is merely distended. The cyst is more frequently extradural than intradural, most commonly unilocular and multiple, and is found on the posterior surface of the spinal cord. The thoracic region of the vertebral canal is most frequently affected, at least in the extradural variety. The cysts often contain daughter cysts. The rapidity of the growth varies greatly, and the symptoms may not become very serious until years after they have appeared.

Hemangioma is very rare; 8 cases only having been reported in the literature thus far. They are extramedullary and very vascular.

Cholesteatomata are very rare growths and present no other characteristic appearance here than elsewhere.

There have been reported in the literature rare cases of spinal chordomata. Henning has given a complete résumé of sacral chordomata. O. Mazzia described a case of a 44-year-old farmer in whom, on operation, a chordoma of the sacral region had been found. There were no symptoms. Feldman describes a sacral chordoma in a woman of 46, which was removed. One year later there was no return. Ribbert believes that one in every two hundred tumors are chordomata, but malignant chordomata are rare. Spinal chordomata are usually metastatic and malignant.

Occasionally cysts arising from the pia and arachnoid, which are probably inflammatory in nature, may contain collections of cerebrospinal fluid; these cysts cause symptoms of compressing the roots of the cord similar to those produced by solid neoplasms. Such collections of fluid cannot be diagnosticated except by operation, and their treatment is identical with that of tumors of the cord.

As far as the *anatomic distribution* of these tumors is concerned, it may be said in general that the most common intramedullary growths found in the cervical region are tuberculomata, gummata and gliomata; the next common in this region are sarcomata, psammomata, fibromata and myxomata. Myxomata and sarcomata are most common in the dorsal region and the next common in this region are the tuberculomata and gummata. In the lumbar region, sarcomata, lipomata, psammomata and hydatid cysts are most common. Here, again, it will probably be found that endotheliomata are more common in the thoracic region, but that they have unquestionably been diagnosed in the past as sarcomata.

In the development of a tumor, the gradual onset and development of symptoms points to a slow growth and therefore to its benign nature, while rapid development of symptoms points to a more rapid growth, and therefore malignant in nature.

The majority of tumors are found to be about 2.5 cm. in length. Lexer removed one of  $17 \times 2.4 \times 2$  cm. On account of the lack of cord in the lumbar and sacral regions of the vertebral canal, growths in these regions have greater opportunity for expansion and therefore may attain an unusually large size.

There may be large collections of spinal fluid both above and below the tumor. In most cases the collection of fluid is above the growth but there are rare cases in which the fluid has been sacculated below. These collections of fluid may give rise to symptoms of pressure, especially upon the roots, in addition to those caused directly by the tumor itself.

In tumors lying externally to the cord, the latter is usually found flattened, or presents depressions opposite the point or points of pressure. The cord may be pale or congested. At the level of the compression the myelin is broken up and the axis cylinders disappear. The blood-vessels are surrounded by proliferations of connective tissue, so that the affected segment of the cord is almost sclerosed. Above and below this level there is an ascending and descending degeneration. The cells of the gray matter, at the point of pressure, are either completely absent or atrophied. The meninges are usually found thickened and adherent.\*

Of late, several procedures have come into general use which facilitate greatly the diagnosis of spinal cord tumors, especially aiding in the differential diagnosis between intramedullary and extramedullary spinal cord neoplasms.

Of these one of the most important tests is the manometric estimation of the spinal fluid pressure with employment of various measures which in normal individuals result in an increase of the spinal fluid pressure as originally described by Queckenstaedt. It is generally accepted now that the normal cerebrospinal fluid pressure varies between 100 and 200 millimeters of water. It will be found that in a patient in complete physical and mental rest, the vast majority of readings will fall within these figures. It is for this reason that the estimation of the pressure of the cerebrospinal fluid should be done several minutes after the insertion of the lumbar puncture needle in order to secure the necessary relaxation. Pressures above 200 are suspiciously high and demand thorough investigation of the signs and symptoms. Pressures below 100 are occasionally encountered, for which no adequate explanation can be given. It may be of interest to note in passing that in several cases of acute infectious myelitis examined by us, the initial pressures were very low, varying between 40 and 60 millimeters of water pressure.

The estimations of the pressure of the cerebrospinal fluid are done with a needle which is so designed that a graduated manometric tube can be attached to the lumbar puncture needle which will give the readings of the pressure in millimeters. The technic employed in these estimations is essentially the same as employed in the lumbar puncture with the exception that we insist on cocainizing more thoroughly the area of insertion of the needle on account of a larger bore of the needle. The patient lies on his side, head flexed on the chest and thighs flexed on the abdomen with reasonable comfort. It is very important that the lumbar puncture should be done painlessly and the patient not held in a cramped position.

\* The author is indebted to Dr. B. Sachs, Attending Neurologist to the Mt. Sinai Hospital, for his kind permission to utilize the clinical material from his service, in the preparation of this article.

It has been known for a long time that any muscular effort, even coughing, straining, sneezing, laughing or crying, results in an increase in the cerebrospinal fluid pressure. Compressing the veins of the neck by interference with the venous outflow from the intracranial cavity also causes a rise in the intracranial pressure and secondarily in the cerebrospinal fluid pressure.

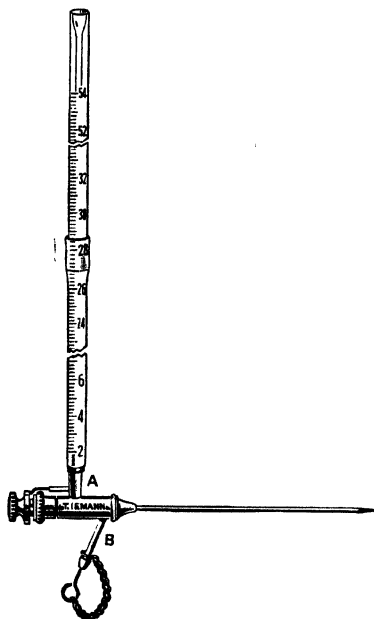


FIG. 10.—THE AUTHOR'S NEEDLE SHOWING THE GRADUATED MANOMETRIC TUBE ATTACHED. Fluid for examination can be obtained through opening *B*, and intraspinal injections can be made by attaching a syringe or gravitation cylinder to the end.

It was Queckenstaedt who first noted that, when the subarachnoid space is obstructed, the usual rise in the cerebrospinal fluid which follows compression of the veins of the neck does not occur with the same promptness and to the same extent as when the subarachnoid space is free. Usually a slight pressure exerted on the veins of the neck results immediately in a prompt rise in the pressure of the cerebrospinal fluid which can be readily observed in the manometer. There seem to be several factors involved in the pressure of the cerebrospinal fluid. Coughing, sneezing and straining cause a rise both in intracranial and in intraspinal pressure by interference with the vertebral and spinal venous circulation. Jugular compression, on the other hand, causes a rise in



the intracranial pressure only due to interference with the venous outflow of blood from the brain.

These observations led to the employment, as a routine, of a series of tests which are employed whenever a spinal cord tumor is suspected. The procedure employed at the Neurologic Service of the Mount Sinai Hospital is as follows: A patient is lying on his side and the area of the fourth lumbar intraspinal space is thoroughly infiltrated, both intradermally and intramuscularly, with 1 per cent. novocaine solution freshly prepared. A lumbar puncture needle is inserted into the fourth lumbar intraspinal space until it pierces the dura and stops in the subarachnoid space. Manometric glass tubes are attached to the "needle" and the pressure reading is taken. The patient is asked to cough, and the rise of the spinal fluid in the manometric tube is noted. Then the patient is asked to relax, and after this has been made certain the patient is asked to strain (as if in a bowel movement) while the reading is noted in the manometric tube. While the assistant or the nurse is asked to press gently the jugular veins on both sides, the reading of the manometer is also taken.

It is quite important to be certain that the tip of the needle is in the subarachnoid space, that the fluid flows freely and that there is no mechanical external interference with the flow of the spinal fluid in the needle by small impurities, small clots of blood or other foreign matter.

In a normal case one usually finds an original pressure of 100 millimeters water pressure. On coughing or sneezing the pressure of the fluid rises to 200 or 300 millimeters water pressure, and on jugular compression the rise reaches 400 or 500 millimeters. Equally important is the rapidity with which the fluid rises in the manometric tube as well as the physical characteristics mentioned previously. An extremely slow rise with absence of respiratory manometric variation indicates some obstruction either in the subarachnoid space or the needle. Any delay in promptness of rises and absence of significant rises is in itself suspicious, demanding further investigation of the patient's condition and possibly application of other diagnostic methods.

Ayer introduced a valuable method in 1921 by combined cistern and lumbar puncture. A dynamic study of the cerebrospinal fluid circulation within the spinal subarachnoid space led Ayer to believe that normally the subarachnoid space affords free communication to fluid. If two manometers are placed at each end of the subarachnoid space, say at the cephalic and caudal ends, one can demonstrate the continuity of the space by lowering or raising the pressure at either end and reading the effects on the manometers. The means for changing the pressure are essentially those as originally described by Queckenstaedt, such as coughing, sneezing, grunting, straining and especially jugular compression which would raise the pressure of the fluid in the subarachnoid space. On the other hand, withdrawing several cubic centimeters of fluid would lower the pressure. This could be demonstrated in both manometers. It stands to reason that if there is any obstruction of the subarachnoid space, continuity of the subarachnoid space is blocked, and while the

manometer at one end will show the effect of the various measures outlined leading to increase and decrease in the pressure of the spinal fluid, the manometer at the other end will fail to show the parallel physiological variations.

Ayer places his patients on one side so that the points of puncture—cistern and lumbar—shall be on the same horizontal plane. A lumbar puncture needle, to which a manometer is fitted, is inserted into the cisterna magna and another needle into the lumbo-subarachnoid space. The fluid is allowed to run into the respective manometers and readings are made. The patient is induced to inspire deeply, cough, sneeze and strain and the oscillations in both manometric tubes are noted. It is especially important to note the oscillations when both jugular veins are compressed.

Then a few cubic centimeters of the fluid are withdrawn from the lumbar needle, permitted to escape and observation is made as to whether the fluid-line drops in the manometric reading of the pressure in the cisterna magna. A few cubic centimeters of the fluid are then permitted to escape from the cistern and the oscillations are noted in the lumbar manometer. By the application of this method in cases with verified cord tumors, Ayer was able to demonstrate the value of the method. Thus in cases of cord tumors, the manometer at the lumbar route failed to register the increase in pressure of the cerebrospinal fluid, when various measures intended to increase the spinal fluid pressure were employed. On the other hand, when several cubic centimeters of fluid were allowed to escape from the lumbar needle, no lowering of pressure was noted in the manometer attached to the cistern needle, thus demonstrating the presence of an obstruction in the spinal subarachnoid space.

Of equal importance is the chemical examination of the spinal fluid withdrawn at both levels. The fluid below the level of the lesion would show a definite chemical difference, especially an increase in the protein content. The gross changes of the spinal fluid below the level of the lesion, its physical characteristics, such as color and specific gravity, together with grosser chemical tests, have been described by Froin. A finer chemical quantitative test of estimation of the protein content of the spinal fluid has been described by Ayer and is especially useful in determining quantitatively the chemical differences in the spinal fluid withdrawn from both levels. Normally, however, the spinal fluid from the cistern level and lumbar level are practically similar. The chemical tests are of special interest in early tumors when the appearance of the fluid below the level of the suspected lesion may give no suspicion of a possible chemical change. The total protein content of the cerebrospinal fluid according to the method of Ayer and Denis is between 15 and 40 milligrams per 100 cubic centimeters.

A somewhat different situation is encountered in tumors of the cauda equina. It is quite frequent that the level of the tumor is below the level of the site of the usual lumbar puncture. In these cases the fluid withdrawn from above the level of the tumor may be distinctly yellow in color and contain large amounts of albumin. A second important ob-

servation pointing to the existence of the tumor is the so-called negative Queckenstaedt; i.e., various readings with a manometer attached to the lumbar puncture needle fail to show any evidence of a block.

The chemical examination of the cerebrospinal fluid withdrawn below the level of the lesion, particularly the estimation of the total protein content, would be of especial value in the so-called cases of adhesive spinal arachnoiditis simulating spinal cord tumor as lately described by Stookey. In these cases, there is no increase in the protein content of the cerebrospinal fluid, and no xanthochromia in spite of a positive manometric test indicating subarachnoid block.

Probably the greatest advance in the diagnosis of spinal cord neoplasm or any form of obstructive spinal cord lesion is afforded by the recently introduced use of lipiodol. Lipiodol is a preparation of poppy-seed oil in which iodine is dissolved in a stable chemical combination. It was originally unsuccessfully used by Lo-Fay for the treatment of epidemic encephalitis. Sicard and his co-workers found that the oil was impermeable to x-rays, and that it was not irritating to the meninges or the parenchyma of the central nervous system. They were the first to inject the oil by spinal puncture, and thereby demonstrate spinal cord obstructions.

Sicard and others have pointed out the following advantages of the method:

1. Lipiodol is an opaque substance easily outlined by the x-ray.
2. Lipiodol injections are remarkably free of painful reactions in spite of the passage of the oil through the maze of the spinal cord roots.
3. Lipiodol is well tolerated by the central nervous system and better still by the meninges.
4. The density of the substance allows it to gravitate, and thus when injected at a higher level it tends to travel down the length of the subarachnoid space and settle down in the sacral cul-de-sac unless arrested by some obstructive process on the way down. The occurrence of such a block serves as evidence of the presence of an agent compressing the spinal cord. This property to gravitate downward may, however, be neutralized by an increase in the adhesive properties of the oil, and this must be guarded against by avoiding errors of technic or else the fluid may adhere to meninges at perfectly normal levels.

As a matter of fact, the oil is not as innocuous to the meninges as Sicard leads us to believe. Both in our clinic and at the Neuro-Surgical Service of the Massachusetts General Hospital, definite meningeal signs of root irritation lasting a few days, especially in a case of intramedullary cord disease, have been observed. But the value of the method cannot be underestimated. One, of course, must remember that lipiodol is not absorbed by the tissues, and probably remains indefinitely in the cul-de-sac. Whether it finally becomes organized it is difficult to say, because the method is still very new and at the time of this writing the first case injected with lipiodol has had this substance for only about six or seven years.

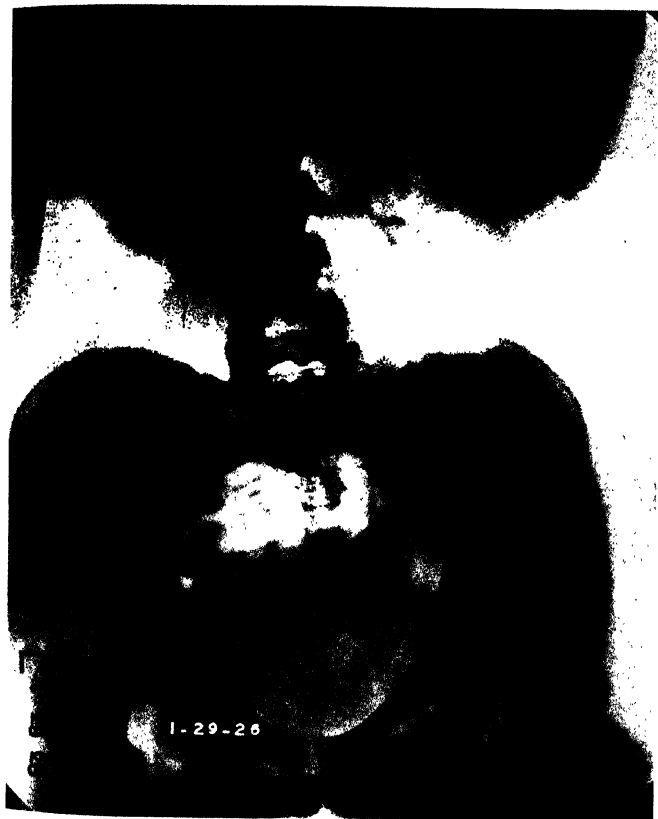


FIG. 11.—LIPIODOL MESHING AT THE LOWERMOST POINT IN THE SUBARACHNOID SPACE IN A NORMAL CASE IN WHICH THERE IS NO EXTRAMEDULLARY LESION CAUSING OBSTRUCTION.

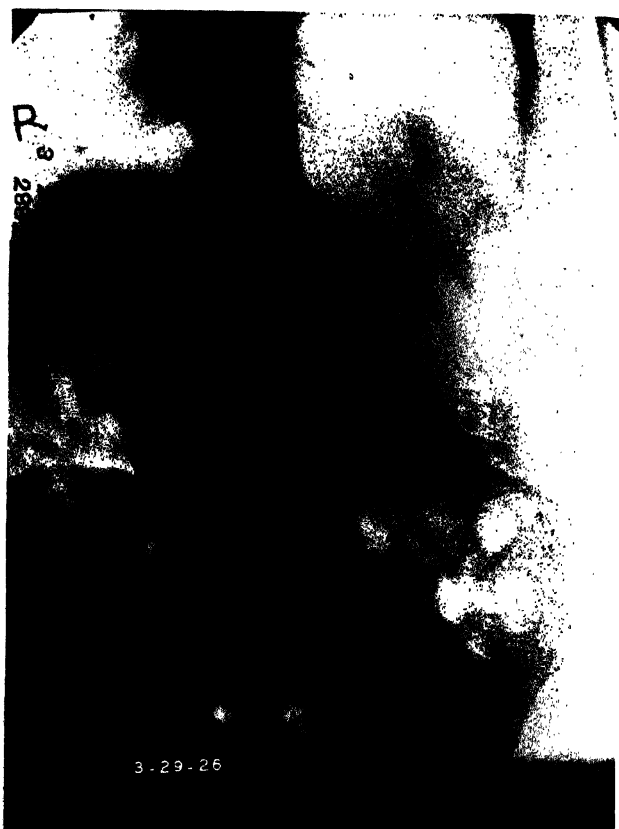


FIG. 12, A.—JOE, AGE 52, COMPLAINED OF SHARP PAIN IN THE RIGHT ILIAC BONE RADIATING DOWN THE LEG, OF 5 MONTHS' DURATION. Pain came mostly at night and was slightly relieved by walking. He had been treated at another hospital for sciatica for 7 weeks without improvement.

Examination showed the following: (1) Bilateral Lasègue; (2) diminished right knee-jerk; (3) atrophy of muscles of right leg; (4) sensory impairment in third and fourth lumbar.



FIG. 12, B.—Queckenstaedt showed rises were small and the fluid dropped slowly, indicating a partial block. The fluid was xanthochromic and showed a pleocytosis of 13.

Diagnosis before lipiodol was arachnitis or neoplasm in the area of L2-3 on the right side.

Lipiodol was arrested at L3, corroborating the clinical findings.

Laminectomy showed the presence of adhesive arachnitis in the cauda equina.

Discharged free from symptoms.



FIG. 13.—LOUIS, AGE 13, COMPLAINED OF INABILITY TO WALK FOR PAST 3 YEARS. OF SUDDEN ONSET ASSOCIATED WITH PAIN IN THE LOWER SPINE. During a period of two years was treated at various hospitals. When attempts were made to correct the foot-drop by means of braces, the diagnosis made was primary spastic paralysis, operation contra-indicated.

Examination showed the following: (1) Spastic paraplegia with pyramidal signs; (2) absent abdominals; (3) hyperalgesia D4-8 with hypalgesia below; (4) vibration diminished below ant. sup. spines; (5) touch intact except few patches on left leg; (6) thermianesthesia below D8.

Diagnosis before lipiodol was extramedullary compression of cord at level D4-6. Lipiodol showed complete arrest at D6, corroborating the clinical findings.

Laminectomy showed the presence of an old Potts abscess with chronic pyogenic meningitis causing compression of the cord.

Discharged unchanged.

There are various technical procedures employed in the intraspinal injections of lipiodol. The one described here has proven to be absolutely safe in a large number of cases and is probably as satisfactory as any. The most important thing to remember is strict asepsis, careful arrangement of details, creating of most favorable condition for rapid and unobstructed diffusion of the oil through the subarachnoid space.

The technic as used in our service is as follows: (1) No cerebrospinal fluid is to be removed by means of lumbar puncture for six to eight days before injection of the lipiodol. All observers agree that it is highly important that no change in the volume of the spinal fluid should take place before the lipiodol is injected if unfavorable after-effects are to be avoided. (2) Patient's back of head and neck should be scrubbed a few hours preceding the procedure. (3) A line is drawn from the bregma downward and posteriorly continuing with the vertebral line. A horizontal line is drawn connecting the lobules of the ears. The point of intersection of the two lines corresponds roughly with the atlanto-occipital ligament. The site of the proposed entrance of the needle is thoroughly cocaineized with a 1 per cent. solution of freshly prepared novocaine. A lumbar puncture needle is introduced through the skin, a distance of six centimeters and no more, piercing the atlanto-occipital ligament and thus entering the cisterna-magna. The dangers of piercing the medulla are, of course, apparent and well known. About 2.5 cubic centimeters of spinal fluid are allowed to escape and then an ampoule containing sterile lipiodol is broken and about 2 cubic centimeters of the clear, air-free lipiodol are injected with an ordinary syringe into the subarachnoid space of the cisterna-magna. Some air is injected afterwards to be certain that all the lipiodol went through the needle. The needle is then withdrawn and the patient, sitting in a wheel chair, is taken to the x-ray room. Twenty minutes are allowed for the lipiodol to trickle down to the cul-de-sac and then x-ray plates are taken. In case the plates show some suspicion of block, another plate should be taken twenty-four hours afterwards. It is best to go through the procedure with the patient sitting up, head and neck as immobile as possible, with lines drawn horizontally and vertically for better orientation of the operator. A preliminary hypodermic of morphine gr. 1/6 and hyoscine hydrobromide gr. 1/150 is advisable. It secures the needed relaxation and rest of the patient.

It is important to remember that the patient should not be in a recumbent position until the x-ray plates are taken, in order for the lipiodol to trickle down the spine. Usually in cases of no block the lipiodol collects in the cul-de-sac within a short time and forms a triangular mass at the bottom of the spinal canal or, as the Germans call it, the "carrot root."

Of the approximately twelve cases which we have observed in the service, two had marked signs of irritation with slight deviations of temperature. The reason why the lipiodol is injected into the cisterna-magna is because it enters the largest free space in the subarachnoid system, and this precludes the possibility of the lipiodol getting stuck to



the meninges at the time of the injection. When the lipiodol has been injected by other observers in the dorsal or lumbar space exactly such a situation took place, i.e., adhesion of the lipiodol to the wall and obscuration of the findings. The lipiodol is specially important in differential diagnosis of multiple sclerosis with a level lesion from cord tumor, in differential diagnosis between extramedullary and intramedullary neoplasm, and in fixing the level of the lesion.

Of course, lipiodol is to be used only as a diagnostic help and its value should not be overestimated. A careful neurological examination pointing to signs of cord compression is the only indication for lipiodol injection. In some cases where there exists evidence of a block as shown by lumbar puncture, the localizing signs of the lesion may be uncertain or even absent. In such cases the use of lipiodol is invaluable.

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## CHAPTER IV

### DIAGNOSIS AND LOCALIZATION OF BRAIN DISEASES

BY ALFRED GORDON, M.A., M.D., F.A.C.P.

#### A. CEREBRAL LOCALIZATIONS

- Introduction, p. 396—Diaschisis, p. 397.
- I. Frontal lobe, p. 397—Prefrontal region, p. 397—Frontal lobe proper, p. 399—Two upper convolutions, p. 399—Third frontal convolution, p. 401—Aphasia, p. 401—Motor aphasia, p. 402—Sensory aphasia, p. 403—Transcortical aphasia, p. 404—Amnesic aphasia, p. 405—Optic aphasia, p. 405—Paraphasia, p. 405—Total aphasia, p. 407—Agraphia, p. 407—Aphasia in right- and left-handed individuals, p. 409—Anarthria, p. 410—Aphasia according to the views of Pierre Marie, p. 412.
  - II. Pre-rolandic area, p. 414—Jacksonian or focal epilepsy, p. 417.
  - III. Post-rolandic area, p. 421.
  - IV. Parietal lobe proper, p. 421—Disturbances of stereognosis, p. 422—Sensory disturbances of cerebral origin: Hemianesthesia, p. 423—Cortical sensory syndrome, p. 423.
  - V. Occipital lobe: Hemianopsia, p. 424—Cortical blindness, p. 429.
  - VI. Temporosphenoidal lobe, p. 430.
  - VII. Mesial surface of the hemisphere, p. 431—Hippocampal region, p. 431.
  - VIII. Basal ganglia, p. 433—Thalamus opticus, p. 434—Corpora striata, p. 435—The red nucleus, p. 439—Corpora quadrigemina, p. 440.
  - IX. Internal capsule, p. 441.
  - X. Corpus callosum, p. 443—Apraxia, p. 445.
  - XI. Cerebral ventricles, p. 448—Third ventricle, p. 448—Hydrocephalus, p. 449—Lateral ventricles, p. 457—Pyocephalia, p. 458—Ventricular hemorrhage, p. 460.
  - XII. Base of the brain, p. 462—Extreme anterior position, p. 463—Interpeduncular region, p. 463—Hypophyseal region, p. 463—The pons, p. 467.
  - XIII. Medulla oblongata, p. 472—Acute superior polio-encephalitis, p. 473—Acute inferior polio-encephalitis (acute bulbar palsy), p. 474—Chronic superior polio-encephalitis (progressive nuclear ophthalmoplegia), p. 477—Chronic inferior polio-encephalitis (labioglossolaryngeal paralysis), p. 477—Pseudo-bulbar palsy, p. 480—Asthenic bulbar paralysis (myasthenia gravis), p. 482—Hemorrhage and softening of the medulla, p. 485—Occlusion of the postero-inferior cerebellar artery, p. 485—Compression of the medulla, p. 485—Tumors of the fourth ventricle, p. 486—Localizing diagnosis of bulbar symptoms, p. 487.

XIV. Cerebellum, p. 488—Cerebellar syndrome, p. 490—Cerebellar hemiplegia, p. 494—Cerebellar parasyndrome, p. 495—Cerebellar tumors, p. 497—Abscess of the cerebellum, p. 500—Cerebellar heredo-ataxia, p. 503—Cerebrocerebellar ataxia, p. 504.

#### B. INTRACRANIAL HYPERTENSION AND TUMORS OF THE BRAIN

Intracranial hypertension, p. 505—Tumors of the brain, p. 510—Treatment of intracranial hypertension and tumors, p. 517—Tumors of the pineal body, p. 520.

#### C. INFLAMMATION OF THE BRAIN AND BRAIN SHOCK

Encephalitis, p. 524—Acute non-suppurative encephalitis, p. 525—Acute suppurative encephalitis (abscess of the brain), p. 528—Chronic encephalitis (cerebral paralysis of children), p. 533—Lethargic encephalitis, p. 545.  
Concussion of the brain, p. 546.  
Nervous disorders following violent explosions, p. 548.

### A. CEREBRAL LOCALIZATIONS

#### INTRODUCTION

For a long time no constant relation was recognized as existing between the seat of a lesion in the brain and the symptoms which may be manifested. Flourens,<sup>1</sup> the great pioneer in cerebral physiology, expressed the views formerly held by saying that "all the cerebral lobes participate simultaneously in the display of brain functions." However, this same author was the first to mention the term "localization" when he speaks of "*noeud vital*," as the seat of the principle of life, localized in the calamus scriptorius.

Soon careful clinicians observed that certain facts could no more be explained except on the assumption of a distinct differentiation of function in the brain substance. An array of distinguished anatomists, biologists, clinicians and experimenters commenced to come forward with facts, all tending to imply that the brain possessed certain special and circumscribed areas, each of which corresponded to a definite psychophysiological function. The names of Broca in connection with aphasia, of Hughlings Jackson with the phenomena of localized epileptiform convulsions of the opposite cerebral hemisphere, of Fritsch and Hitzig, who inaugurated a new era in cerebral physiology by demonstrating experimentally movements on one side of the body when the surface of the opposite cerebral hemisphere was being irritated (by electric currents), the names of Ferrier, of Franck and Pitres, of Dupuy, of Carville and Duret, of Richet—these are but a few among many others who kept on contributing more and more facts towards the general acceptance of the doctrine of cerebral localizations.

At the present time this doctrine is considered as pretty well established, and with increasing experience it has acquired great significance

from a practical standpoint, viz.: exact surgical intervention. Although it happens occasionally that pathological findings do not correspond precisely to the clinical manifestations, they do not, however, invalidate the fundamental principles of special functions depending upon special circumscribed areas of the brain. These exceptions are not genuine contradictions, as, with gradually increasing knowledge in the domain of cerebral physiology, we are enabled to give more adequate interpretations to apparently embarrassing observations. As an illustration of this contention, attention may be called to the theory of **Diaschisis** (*διά*, apart, + *σχιζειν*, to split), advanced recently by von Monakow and based upon the experimental work of Loeb. The latter maintains that a limited cerebral lesion cannot destroy the whole function, but only certain elements of it, and that in such cases the disturbance is due to the dynamic influences exerted by the lesion on associated and distant areas. Parting from this conception, von Monakow<sup>2</sup> has worked out his theory on Diaschisis.\*

In presenting the vast subject of Cerebral Localizations based upon our present knowledge, the following plan will be adopted:

1. Individual Convolutions and Lobes of the Cortex will be discussed *seriatim*, beginning from the Frontal Lobe posteriorly.
2. The Base of the Brain.
3. The Structure of the Interior of the Brain.
4. The Cerebellum.

## I. FRONTAL LOBE

### A. PREFRONTAL REGION

The anterior portion of the frontal lobe, called prefrontal lobe, has been recognized since Goll as the preponderately better developed in highly intellectual individuals. Pathologic and experimental studies have shown that a tumor or any lesion of the prefrontal region, particularly in the left hemisphere, is more frequently attended by mental disturbances than a lesion of any other portion of the brain, except, perhaps, that of the corpus callosum. Ferrier<sup>3</sup> has demonstrated experimentally that, after removal of the prefrontal regions, a decided alteration in the animals' character and behavior takes place: they

\* By a diaschisis is meant a functional shock-like inhibition (passive paralysis) of distant areas produced by dynamic influences of the original lesion anatomically connected with those areas. The connection may be through the fibers of association, projection or the commissural. Through the break of continuity of the connecting paths, the distant portions of the brain, medulla and spinal cord become isolated and therefore, according to von Monakow, they may be in a state of either associative, or commissural, or corticospinal, or corticomesecephalic, etc., diaschisis. As long as the latter persists, the inhibited areas are even unable to perform the functions for which the destroyed regions are not indispensable. But this functional impotence is only temporary; the choked distant areas gradually and progressively free themselves from the state of the diaschisis and resume again their interrupted functions. The permanent disorder is confined only to the directly injured elements.

became apathetic or dull; dozed off to sleep, responding only to the sensations or impressions of the moment and wandering to and fro aimlessly; "they lost the faculty of attentive and intelligent observation." Horsley and Schäfer noted signs of stupidity in monkeys in which the prefrontal regions had been removed. Hitzig<sup>4</sup> and Goltz<sup>5</sup> observed in dogs marked weakness of memory and an inability to fix attention after destruction of the prefrontal lobes. Mental deterioration and a defect of the faculty of attention appear to be the essential disturbances as seen from experimental observations.

L. Welt<sup>6</sup> made a careful study of eight cases with various lesions of the prefrontal lobe and noticed the following mental symptoms: the patient is morose, taciturn, suspicious and at times violent. L. Steven<sup>7</sup>



FIG. 1.—HEMORRHAGE IN THE PREFRONTAL LOBE FOLLOWING TRAUMA.

(From Gordon's "Diseases of the Nervous System," P. Blakiston's Son & Co.)

concludes from his studies that patients thus affected are very facile in temperament, unable to concentrate their attention and present loss of memory for recent events. Bianchi, who made exhaustive studies of the subject, points out the following mental symptoms: restlessness, indifference, irritability, want of criticism, automatism. Flechsig, who places in the frontal lobe one of his association centers, finds in diseases of this area a loss of sense of relation of personal consciousness to outside influences, inability to discriminate possibilities from impossibilities and, finally, loss of self-control. Mabilie and Pitres<sup>8</sup> report the history of a patient who lost the ability of recalling perfectly events of his past life, of living new memories, also of appreciating his present surroundings. Autopsy showed two symmetrical areas of softening, one in each hemisphere, in the midst of the white substance of the prefrontal lobes.

The German writers described a special symptom which they found in a large number of cases in diseases of the prefrontal lobe. Jastrowitz gave it the name of "moria," Oppenheim calls it "Witzel-

sucht." The characteristic feature of this symptom is the humoristic spirit which is seen in the patient's actions and words. Although it was observed in tumors of other areas of the brain, it is nevertheless present most frequently in affections of the prefrontal lobe. (Schuster.<sup>6</sup>) In a case of the writer's, in which at autopsy was found a hemorrhage in the white substance of the left prefrontal lobe, there was during life a state which could be called "euphoria." The patient was happy, everything appeared to him "pretty" or "handsome," he felt as if he were in "paradise," he was always "glad to see everybody."<sup>10</sup> Summing up the experimental and anatomicoclinical observations, the following are the principal manifestations of lesions occurring in the prefrontal lobe: mental hebetude, automatism, excitement and irritability, or else depression, disorientation and loss of power to concentrate attention, lack of self-control, moria and euphoria.

#### B. FRONTAL LOBE PROPER

Two separate portions are to be considered, viz.: (a) the upper and middle convolutions; (b) the third convolution.

##### (a) *The Upper Two Convolutions*

Ferrier<sup>11</sup> severed by a frontal incision both frontal lobes immediately anterior to the precentral sulcus. After rapidly regaining consciousness the animal, though able in some degrees to extend its head and trunk, was unable to maintain the upright position or move its head and eyes laterally. Clinicians have since then observed some symptoms indicating also the possibility of this portion of the brain being concerned with the movements of the head and eyes. Thus convulsions occurring in cases of frontal tumors may be accompanied by conjugate deviation of the head and eyes to the opposite side. Some writers consider the inferior parietal lobule (supramarginal gyrus and the angular gyrus) as the seat of cortical representation of movements of the head and eyes. (Ferrier, Landouzy, Wernicke.) A number of experiments upon higher animals have shown that there are two cortical zones, stimulation of which produces conjugate deviation of the head and eyes. One is anterior or frontal, which is direct; the other posterior, which is due to a lesion of the inferior parietal region indirectly, viz., to an irritation or destruction of the visual or auditory fibers underlying the angular gyrus or the supramarginal gyrus respectively.

Lesions in the frontal lobes may produce symptoms referable to the cerebellum; thus, titubation, ataxia of station, asynergia have been observed. L. Bruns<sup>12</sup> reports four such cases. In Bernhardt's book on *Hirngeschwülste*<sup>13</sup> we find reference to 40 per cent. of frontal tumors with ataxia resembling that of cerebellar diseases. O. Fragnito<sup>14</sup> has recently reported an important case of tumor in the right frontal lobe which developed as a clinical picture of the cerebellar

syndrome. In F. Tilney's<sup>15</sup> case there was a cyst of the frontal lobe with direct posterior fossa symptoms. In a recent publication entitled "Lesions of the Frontal Lobe Simulating Cerebellar Involvement,"<sup>16</sup> the writer presented four anatomicoclinical cases in which a cerebellar diagnosis was justifiable, but the following frontal lobe conditions were

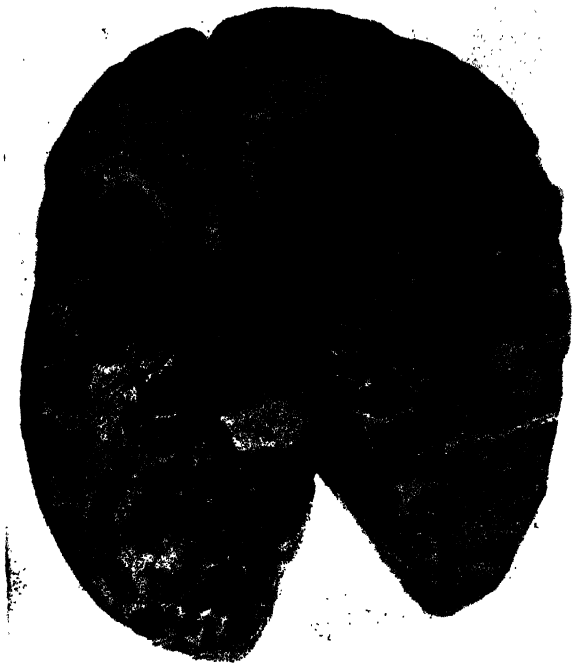


FIG. 2.—TUMOR (ROUND-CELL SARCOMA) WEDGED IN BETWEEN THE LEFT FRONTAL INSULA AND TEMPORAL LOBES, PENETRATING THE LATERAL VENTRICLE.  
(Gordon, Courtesy *Journal of Mental and Nervous Diseases*.)

found: cystic cavities in the first case, a sarcoma in the second, an abscess in the third and a hemorrhage in the fourth case. It is therefore important to determine the differential diagnostic features between cerebral and cerebellar affections. They will be discussed in the section on Cerebellar Localizations.

Among other special symptoms observed in lesions of the frontal lobes, those described by Grainger Stewart<sup>17</sup> are to be mentioned. He claims that diminution or absence of the contralateral abdominal re-

flex and the presence of a homolateral vibratory tremor are suggestive of tumor of the frontal lobe.

Finally, the second frontal convolution (its foot) has been considered by some observers as the center of the faculty of writing. Exner, in 1881, was the first to claim the existence of such a special graphic center. As the subject of agraphia is intimately associated with the problem of aphasia, it will be discussed in the next section.

### (b) *Third Frontal Convolution*

In this area lies the center of speech as enunciated by Broca in 1861. A lesion of this portion of the brain produces aphasia. In spite of the fact that certain forms of speech disorders are due to an involvement of areas other than the third frontal convolution (Broca's region), nevertheless, for the sake of completeness, the subject of aphasia will be discussed here in its entirety.

### APHASIA

In order to communicate an idea, two elements are necessary, viz., comprehension and expression of it (verbally or graphically). Aphasia, therefore, may be: *sensory* and *motor*.

In the history of the problem of aphasia we observe three periods. In the first period the teaching of Broca remained intact. Aphasia was then understood as a disorder in which the articulated speech was altered. Trousdale claimed also that such patients are incapable of understanding what they read and of writing spontaneously. Bastian, in 1869, was the first to call attention to the fact that some aphasics could not understand spoken words.

With Wernicke (1874) commences the second period. He admits two centers of speech: one, frontal, which is the Broca's area for articulated speech; the other, posterior, which is located in the first temporal convolution and is the center of auditory images. The latter regulates the former, as in case of a lesion, the patient, while being able to pronounce words, is nevertheless unable to use them properly. Dejerine, in 1881, reported a case of word-blindness, and a lesion was found in the angular gyrus. Exner, in the same year, claimed a center for writing and placed it in the foot of the second frontal convolution.

Thus four centers of speech were considered: a center of motor aphasia (Broca's area); a center of word-deafness (Wernicke's area, in the posterior portion of the first temporal convolution); a center of word-blindness (angular gyrus); a center of agraphia (second frontal convolution). The latter has been strongly contested. Bastian, in 1898, has shown that all the four speech centers are intimately connected with each other and that the auditory center plays the most important rôle in the mechanism of articulated speech.

The third and last period in the history of aphasia is characterized by a totally new conception of speech disorders. P. Marie, the author



of it, announced, in 1906, that there is but one form of aphasia, that there are no special centers for word-deafness and word-blindness, that the latter are due to an intellectual deficit which accompanies all forms of aphasia, that Broca's aphasia is a sensory aphasia, due to a lesion of Wernicke's zone plus anarthria, that Broca's region plays no part whatever in the function of speech, that the area involved in aphasia occupies the so-called "lenticular zone."

The newer view on aphasia as advanced by Marie has many adversaries but is not accepted by the majority of writers. It will be discussed in detail after a description of the classical doctrine of aphasia has been presented.

**Motor Aphasia (Broca's Aphasia).**—Two varieties are possible: either the inner language is altered or it is not altered.

(1) **MOTOR APHASIA WITH ALTERATION OF THE INNER LANGUAGE.**—Here the essential characteristic lies in a partial or total loss of spontaneous speech, hence in an inability to express the thoughts by speech. Either the patient can pronounce only certain words, or only one or two words, and he frequently repeats the same words. Another patient has his vocabulary limited to the word "yes" or "no." In other cases we observe that the patient is able to use only very short sentences. Finally, in very mild cases, the patient is capable of speech, but in the midst of the conversation he stops, being unable to recall the word or sentence desired. With the disturbance of speech, not infrequently the intonation of the voice is found to be altered: it does not correspond to the nature of the thought which the patient seeks to express; he has lost the power of modulating his voice while speaking. On the other hand, in singing, some aphasics are able to use the voice properly and are even able to pronounce the words sung, but should they attempt to recite or read them, difficulty will be evident.

The disorder described is observed not only with regard to spontaneous speech, but also to reading and repeating words. As to the difficulty of reading aloud, the impression may be that the patient has word-blindness (*see* section on Alexia); a close analysis, however, will show that he understands individual words, but has difficulty in grasping the meaning of sentences. It is the "association" of words which is defective, a fact upon which Dejerine especially repeatedly insisted. Besides, the disturbance of reading is very rarely persistent; it gradually disappears, but the patient remains a motor aphasic. The same remarks may be made with reference to words spoken: at first, the aphasic understands when he is spoken to, but later he does not fully grasp the meaning of sentences spoken. However, there is no genuine word-deafness (*see* elsewhere in this section), as rapidly this disorder improves and finally disappears.

The faculty of "writing" is always affected in motor aphasia, but only in the spontaneous variety of it and under dictation; the copying, however, is invariably preserved.

Thus it is evident that, while all varieties of speech are more or less involved in Broca's type of aphasia, nevertheless the predominance

of the **speech disorder** is to be found in the pronunciation of words; the accompanying disturbance in hearing and reading words is but slight and it eventually disappears. The other characteristic is the defective association of words; otherwise speaking, the mental picture of phrases and sentences is deficient or the inner language is altered.

(2) **MOTOR APHASIA WITH INTEGRITY OF THE INNER LANGUAGE, OR PURE MOTOR APHASIA** (*Aphemia*).—Charcot, Pitres, Lichtheim and especially Dejerine are the first writers who gave anatomicoclinical proofs of the existence of this disorder. We find here the same disturbance of the spontaneous speech as in the first variety of aphasia, except that the mental image of articulation of words is intact, the inner language is preserved; such a patient will in various ways show that he knows the number of syllables or letters in each word. In Lichtheim's case he pressed the examiner's hand as many times as there were syllables; in Dejerine's cases the patients made as many efforts of expiration, or showed on the fingers as many times, as there were syllables or words. Evidently the mental reading is here normal.

Pure motor aphasia may make its appearance either at the outset of an apoplectic attack or else it may develop some time after the typical Broca's cortical aphasia has been in existence. In the latter case, the pure aphasia may be considered as a phase of improvement in the course of cortical aphasia.

The preservation of the inner language explains the fact that patients with pure motor aphasia are able to write spontaneously and under dictation, contrary to what is observed in the first variety of aphasia in which this faculty is defective because of the defective inner language.

The anatomical substratum of pure motor aphasia was supposed at first to consist of an involvement of the subcortical tissue in Broca's area, thus separating the latter from its connection with the opercular region which is the motor center of the muscles of lips, tongue, larynx and pharynx, all participating in the mechanism of articulate language. Subsequent autopsies have demonstrated that such a limitation of lesion is not always the case, that there are cases with involvement of both cortical and subcortical tissues. The difference, consequently, between the two varieties of motor aphasia is to be found in the condition of the inner language.

**Sensory Aphasia.**—In sensory aphasia two faculties are affected, viz., the ability to understand words *heard* or *seen*.

(1) **WORD-DEAFNESS** (*of Wernicke*).—Word-deafness is characterized by a loss of understanding words spoken. The degree of loss varies from one case to another; in slight forms only certain words are not understood; in more pronounced cases there may be a loss of comprehension of the most ordinary words; in severe cases the patient is absolutely unable to respond to questions asked of him; spoken language appears to him as being foreign. The easiest way of testing the degree of involvement is to ask the patient to execute certain acts, such as placing an object, going to a place, sitting down, etc. The pa-

tient's inability to carry out a given order will show at once his word-deafness. There may be deafness not only to words spoken but also to musical sounds, so that the patient is unable to distinguish familiar pieces of music. *Amusia* is therefore a variety of word-deafness.

*Subcortical Word-deafness.*—Described first by Lichtheim, in 1884, it is characterized by an inability to understand words spoken aloud, to repeat words and to write under dictation. Spontaneous speech, spontaneous writing, reading aloud and writing by copying, are all intact. Evidently the inner language is preserved. The seat of the lesion is in the subcortical tissue of the temporal lobe, the cortical center being intact. In all such cases one must make certain that the auditory apparatus is not involved, especially the labyrinth, as a lesion of the latter may give an identical symptomatology. Dejerine calls subcortical word-deafness *pure word-deafness*.

(2) **WORD-BLINDNESS.**—Word-blindness is characterized by an inability to read written or printed letters and words (alexia), although the patient is able to distinguish the shape, appearance or other details of the letters. As in word-deafness, we observe here all degrees of involvement, from an impossibility of recognizing one single letter to the ability to read some words. In some cases the patient may not be able to read notes of music (music-blindness). As a rule, in cases of word-blindness, the ability to recognize figures is preserved so that mathematical calculations are possible. In some cases the patients are able to read at first, but soon they cease to comprehend the meaning of the words. This condition was described by Berlin and Bruns under the name of "dyslexia."

*Pure Word-blindness.*—Described first by Dejerine in 1892, it consists of a loss of ability of mental reading and of reading aloud. The spontaneous speech, repeating words, understanding spoken words, spontaneous writing and writing under dictation, are all well preserved. Otherwise speaking, the only language faculty lost is the *reading*. The inner language is therefore intact. Pure word-blindness may present various degrees: it may be total or partial. Loss of power to distinguish musical notes is usually present. According to Dejerine, the power of recognizing mathematical figures is preserved. A right lateral homonymous hemianopsia is usually present. The latter finds its explanation in the anatomical findings which consist of a lesion in the subcortical fibers connecting the angular gyrus with the center of general sight.

**Transcortical Aphasia.**—Wernicke described under this name a form of aphasia which is characterized anatomically by an interruption of connection between the centers of speech and the remaining cortex cerebri, while the speech centers themselves as well as their reciprocal connections are intact.

The essential clinical characteristic consists of preservation of the faculty of *repeating words*.

Wernicke considers a *motor* and a *sensory* variety.

In the *motor* transcortical aphasia the patient, in repeating words or sentences or in singing, articulates words with greater facility than

in spontaneous speech. Likewise the faculty of writing under dictation is intact, while that of spontaneous writing is greatly altered.

In the *sensory transcortical aphasia* there is loss of comprehension of spoken words and there is paraphasia (*see below*) in spontaneous speech, but repetition of words spoken and writing under dictation as well as singing are all correct. The repetition of words is done parrot-like without understanding their meaning (*echolalia*).

The existence of transcortical aphasia as a separate entity is somewhat doubtful, as it has been observed in lesions of Broca's region and of the insula, as well as in those of the temporal and occipital lobes.

**Amnesic Aphasia or Verbal Amnesia.**—This consists essentially of an inability to find the name of an object asked to be named. The patient has no motor or sensory aphasia; he speaks correctly and spontaneously, is even able to describe the properties and usage of the subject, but he is utterly incapable of naming it. On the other hand, if wrong names are given to the object the patient will not accept them until the correct one is mentioned and then he will repeat it correctly. However, it frequently happens that the patient soon forgets its name and when the same object is shown him again a few minutes later, he will experience the same difficulty in recalling it. Verbal amnesia is commonly met with in motor and sensory aphasia, especially during convalescence when there is great improvement in the speech disorder.

The loss of faculty of recalling names of objects in connection with aphasic disturbances must not be confounded with an analogous condition observed in cases of general disturbances of cerebral functions, such as in cranial traumata or in senile dementia.

**Optic Aphasia.**—Like verbal amnesia, it is characterized by an inability to recall the name of an object presented, although the patient knows the properties and usage of it. But if he cannot name the object by looking at it, he can do so by handling it, by palpating, touching, smelling or tasting it. Otherwise speaking, the visual image alone is not sufficient to bring out the articulating image of the object, but other images are indispensable, namely, tactile, olfactory and gustatory. This disorder is rarely observed and only in association with sensory aphasia. Closely allied to optic aphasia is a phenomenon called "psychic blindness" which is characterized by an inability to recognize surrounding objects and persons. An individual affected with this condition must always be accompanied by some one on the street and in the house, as otherwise he will get lost and meet with accidents.

**Paraphasia.**—This character of speech in *sensory aphasia* deserves special mention. First of all, while in motor aphasia the patient either does not speak at all or uses very few words and always the same words, in sensory aphasia the patient usually speaks very much. In the latter case, since the auditory center is involved, the patient loses the regulator of his speech: either he will use strange words which only resemble the words he wishes to pronounce or else he will substitute new words which have no relation to the original idea. His speech is then unintelligible and while the pronunciation of words is

correct, they have no meaning whatsoever (paraphasia). In a patient who presented alexia and verbal amnesia due to a destruction of the lenticular zone (of Marie) there was paraphasia: asked to read, "Saturday Evening Post," he read, "Sanitarium Evening Postal"; asked



FIG. 3.—GLIOMA OF THE PARIETAL LOBE DESTROYING THE LENTICULAR ZONE AND PRODUCING PARAPHASIA.

(Gordon, Courtesy *Archives of Internal Medicine*.)

whether he was happy, he answered: "I have the old folks; I don't owe anybody."<sup>18</sup>

An individual suffering from word-deafness may not hear his words at all or else hear only some words. The paraphasia may therefore be

pronounced or slight. For the same reason repeated words are also defective. Similarly in singing paraphasia will be evident for the words used. When word-blindness is present, the patient will not be able to read aloud, as he does not understand the meaning of the words; but should he be able to understand some words or sentences, the language will be abnormal and paraphasia will be manifest.

**Total Aphasia.**—Aphasia is *total* when there is a combination of symptoms of motor and sensory aphasias, and pathologically the entire language zone is involved. Ordinarily in such cases there is also present a hemiplegia on the right side. Total aphasia is very frequent, but it is not persistent in the majority of cases. Usually word-deafness improves and eventually disappears, while motor aphasia, word-blindness, and sometimes *agraphia* remain with the patient. In some cases the word-blindness gradually improves and the total aphasic becomes a motor aphasic; as such he may remain permanently or else improve and even make a complete recovery. The symptom-group of total aphasia must not be confounded with that of Broca's aphasia in which during the first few days after its onset there are also some evidences of word-blindness and word-deafness, but the latter rapidly disappear. In such cases there is no lesion of the sensory centers of speech, but only an inhibitory influence at a distance, while in cases of total aphasia there is a genuine lesion in those centers.

To sum up, in total aphasia there is a complete abolition of speech. The patient is unable to pronounce words spontaneously, to repeat or to read; word-blindness and word-deafness, also *agraphia* for spontaneous writing, copying, and writing under dictation are all total. Finally, there is a very marked intellectual deficit, even more pronounced than in sensory aphasia.

**Agraphia.**—Disturbance of the faculty of writing is a common accompaniment of aphasia. In studying any case of *agraphia* it should be borne in mind that a motor aphasic, who is at the same time hemiplegic, may not be able to write because of the paralysis of the arm and hand. Consequently an aphasic whose writing is defective will be considered *agraphic* only when he retains a sufficient amount of power and sensations in the hand for executing fine acts such as buttoning, sewing, etc.

The act of writing may be *spontaneous*, *copying*, and under *dictation*. The first and the last forms are usually involved in aphasia; copying is, as a rule, preserved. Like aphasia, *agraphia* may be *total* or *partial*. An *agraphic* may not be able to write a single word or write only a few familiar words, such as names. Sometimes the patient is able to write individual letters, but when he attempts to combine letters or syllables, the result is analogous to what we observe in paraphasia, namely, there is no meaning in the combination of the letters. The condition is then "*paragraphia*."

When the writing under dictation and the spontaneous writing are abolished, the patient may be able to copy. Curiously enough, some patients will be able to copy only by reproducing exactly the type of printed or of written letters. In other cases the spontaneous writing and that

under dictation are intact, but the copying is lost or difficult. In cases of *agraphia* associated with motor aphasia the patients are able to make small mathematical calculations on the paper but not complex ones. Only in pure or subcortical aphasias (*see* above) the faculty for mathematical calculations is totally preserved, because, as Dejerine explains it, the interior language and, consequently, intelligence are preserved.

**AGRAPHIA IN MOTOR APHASIA.**—In this condition spontaneous writing and writing under dictation are altered. In mild cases the patient may be able to write individual words or parts of sentences. In other cases the patient may write his own name or familiar names, but his writing is done mechanically. Outside of this he is unable to present his thoughts in writing.

The power of copying is intact. In some cases it is done in precisely the same form of letters as the original is printed or written. In other cases the form of letters is not exactly reproduced, so that printed letters are presented in written letters.

**AGRAPHIA IN SENSORY APHASIA.**—As in the preceding form, outside of his own name the patient is unable to write spontaneously; he is *totally agraphic*. Occasionally there may be *paragraphia*; individually the words are correct, but collectively they are without a meaning. The patient is unable to correct his writing because of his word-blindness.

Writing *under dictation* is impossible because of his word-deafness and, if occasionally he may hear some words, he writes them down again without any constructive meaning. *Copying* is difficult. If the patient makes an attempt to do it, he does it very slowly; he copies the letters as if they were artistic figures; he may spend several hours on a few words. If, while he is copying and before he has finished a letter or a syllable, the original writing is withdrawn, the patient will not be able to continue the writing.

**AGRAPHIA IN TOTAL APHASIA.**—*Agraphia* in total aphasia is of the same character as in sensory aphasia. The *course* of *agraphic* disorders is dependent, generally speaking, upon the evolution of the symptoms of aphasia. Amelioration or recovery of the latter is accompanied by a similar condition in the symptoms of *agraphia*. Exception should be made in cases of hemiplegia, which, if persistent, will interfere with the power of using the hand for writing in spite of the recovery of speech. In such cases the other hand may be trained for writing.

In *motor aphasia* the patient will recover his faculty of writing completely if the speech is totally recovered. In *sensory aphasia* the disturbances of the faculty of writing are never entirely removed, because complete recovery from speech disorder rarely occurs. In the *subcortical* or pure forms of aphasia, *agraphia* is absent. It is, therefore, evident that disturbances of writing will be present whenever the *inner language* (*see* above) is altered.

**LOCALIZATION OF AGRAPHIA.**—There are a few *anatomicoclinical* cases in the literature which tend to corroborate the conception of a separate center for writing as advanced first by Exner in 1881, namely, in the posterior portion of the left second frontal convolution. In Gordinier's case

(1899), for example, there was a slight paresis of the right arm, agraphia, but no aphasia. There was a progressive development of mental hebetude. Autopsy showed a subcortical tumor in the second frontal convolution extending into the prefrontal region, the first frontal and below to the frontal cornu of the lateral ventricle. Although in this case the conspicuous lesion was at the level of the second frontal convolution, nevertheless it was not strictly cortical and it was too extensive to speak of localization. On the other hand there are far more examples in the literature which speak against the above graphic center. Such is the observation of MacBurney and Allen Starr, in which they report a tumor in the posterior portion of the left frontal convolution involving also the adjacent portions of the first and ascending frontal convolutions. The patient presented during life no aphasia and no agraphia but mental hebetude. Such was also one case of Byrom Bramwell with exactly identical findings. Particularly striking is the case of Bar published in 1878: the patient was aphasic and agraphic and the lesion (tumor) was strictly confined to the cortex of the left second frontal convolution, but when the patient regained his speech, his faculty of writing also returned. Had the tumor been in the alleged center of writing, destruction of the latter would have been followed by a permanent agraphia, which was not the case.

As another example of the untenability of the view concerning a special center for writing, may be mentioned the fact that, in many instances, spontaneous writing is affected while the act of copying is preserved (*see* Sensory Aphasia). If a center of writing is involved, all varieties of writing must be disturbed. Clinical observations and pathological investigations prove that disturbances of writing run parallel with disturbances of speech and that the former is the result of changes in the inner speech (*see* Aphasia). Such a patient, not possessing full knowledge of the meaning of words and consequently being unable to bring out their corresponding visual images, is herewith incapable of tracing them on paper. A special center for writing cannot be admitted in the same sense as the Broca's center for speaking.

**Aphasia in Right- and Left-handed Individuals.**—The largest majority are right-handed. Aphasia in them is due to a lesion in the left hemisphere. It is frequently associated with a right hemiplegia. Aphasia in left-handed individuals is due to an involvement of the right hemisphere. It is associated with a left hemiplegia.

In both cases, but especially in the latter, the opposite hemisphere may supplement to a certain extent the deficit of the involved one. Dejerine cites a case of a middle-aged woman—left-handed—who presented a left hemiplegia and total aphasia with agraphia. In four years she recovered her speech entirely and only partly her power of writing. While she was left-handed for all kinds of work, she nevertheless trained herself to use her right hand for writing. While at autopsy there was a marked lesion in the right hemisphere, thus explaining her left hemiplegia and aphasia, nevertheless the left hemisphere was called



upon by her in developing the faculty of writing with the right hand. In exceptional and very rare cases (Oppenheim, Lewandowski, Mendel) right-handed individuals presented aphasia with left hemiplegia and the lesion was found in the right hemisphere. In *ambidextrous* individuals the special centers of both hemispheres participate in speech so that if one of them is involved the other produces compensation—the individual rapidly regains his lost or impaired faculty.

**Anarthria.**—Under this name is understood a mechanical inability or difficulty (dysarthria) of articulating words, because of a disorder in the muscles of phonation, viz., tongue, lips, palate and pharynx. The disorder may be paralysis, spasm or atrophy. It is therefore evident that there is nothing in common between anarthria (or dysarthria) and motor aphasia clinically and anatomically. An aphasic has a very restricted vocabulary; he may be able to pronounce one or two words slowly, but he does it correctly. An anarthric pronounces badly every word and his language cannot be understood. An aphasic *does not know* how to speak, an anarthric *cannot* speak. If in the latter case some words are still pronounced, although poorly, we speak of dysarthria.

As to the character of speech in dysarthria, it depends upon the nature of involvement of the muscles of phonation. In case of spasm, the speech will be explosive and incoördinate. Should the muscles of the lips be paralyzed, the difficulty will be observed in the pronunciation of labial letters; if the muscles of the tongue are involved, the dental letters will be affected. Generally speaking, the consonants are poorly pronounced, the vowels remain intact.

**PATHOGENESIS.**—The muscles of phonation, namely, those of larynx, pharynx, lips, tongue and palate, are supplied by the seventh, ninth, tenth, eleventh and twelfth cranial nerves. Their nuclei, which are located in the medulla, are connected through a system of neurons with the anterior portion of the operculum of the rolandic area. (Grünbaum and Sherrington.) These neurons originate in the operculum, pass through the centrum ovale to the knee of the internal capsule, descend in the inner portion of the foot of the crura, decussate lower down and terminate at the above-mentioned nuclei. We have therefore two systems of neurons controlling the phonetic apparatus: one from the brain to the medulla, the other from the medulla to the muscles. It is evident that a lesion of any portion of the neuron systems, from the opercular cells to their terminations in the muscles or of the muscles themselves, will result in dysarthria or anarthria. Horsley and Beever have shown experimentally that the operculum, which is the cortical center of the inferior portion of the seventh nerve, of the twelfth nerve, of the masseteric nerve, and of the muscles of phonation, has a bilateral action on the muscles of the tongue and on the muscles of mastication and phonation (on the seventh nerve the action is chiefly crossed). In view of this bilaterality, a persistent and marked dysarthria or anarthria will follow a bilateral involvement of either of the two systems of neurons, viz., operculobulbar and bulbomuscular.

**DISEASES IN WHICH DYSARTHRIA IS OBSERVED.**—1. *Pseud. bulbar*

*Paralysis of Cerebral Origin.*—Dysarthria is here one of the most conspicuous symptoms. It is associated with dysphagia and paralysis of the palate. The voice is nasal; the labial and especially guttural letters are badly pronounced. The speech is of an explosive character, so that the phrases are frequently interrupted and are monotonous. In pronounced cases the speech is not understandable at all. The dysarthria in pseudo-bulbar cases makes its appearance suddenly, while in true bulbar paralysis it develops slowly and progressively. In doubtful cases the following differential symptoms may serve as a guide in making a diagnosis of either of the two affections. In bulbar paralysis (the labioglossolaryngeal paralysis of Duchenne) which is due to a nuclear involvement in the medulla, the tongue is first affected; the involvement of the lips is next in order, then the palate and pharynx are paralyzed; finally the muscles of the larynx become affected. Paralysis and rapid atrophy of all these muscles are striking, fibrillary contractions soon make their appearance. In accordance with this order of events the consonants, guttural and dental, disappear first from speech; then the labial letters and the vowels *o* and *u*; finally, the letter *a* can no more be pronounced. When the larynx becomes involved, there is no longer dysarthria, but complete anarthria. In pseudo-bulbar paralysis the course of the disorder is different. The dysarthria is not slow in developing, but sudden, because of the simultaneous involvement of the entire apparatus of phonation. Atrophy and fibrillary contractions of the affected muscles are absent. Besides, there is usually a bilateral hemiplegia (or hemiparesis) of a spastic character; finally there is an intellectual deficit which is evident from the increased emotivity manifesting itself in spasmodic attacks of laughing and crying.

2. *Bulbar Paralysis.*—The dysarthria with muscular atrophy of the apparatus of phonation (*see* preceding section) may develop in the course of, or more frequently as a termination of, amyotrophic lateral sclerosis.

3. *Syringomyelia of Bulbar Form.*—Here the dysarthria and other symptoms are similar to those of bulbar paralysis. Moreover, there will be also special sensory disturbances of the face over the area of distribution of the fifth nerve (syringomyelic sensory dissociation). There will be also myosis, narrow palpebral fissure and enophthalmia.

4. *Bulbar Paralysis with Acute Course.*—It may be due either to a hemorrhage, embolism or thrombosis of the basilar or vertebral arteries, or else it is due to an *acute inferior* polio-encephalitis. If the polio-encephalitis is simultaneously *inferior* and *superior*, in addition to dysarthria and dysphagia, there will be also paralysis of the muscles of the eyes and of the superior facial nerve.

5. *Anterior Poliomyelitis.*—The nuclei of the medulla may become involved especially in the epidemic form of poliomyelitis. Dysarthria and dysphagia and other symptoms of bulbar paralysis will be present from the onset of the disease. The latter is in such cases sudden and of great intensity. Death is frequent.

6. *Myasthenia Gravis.*—Dysarthria is present because of the in-

vovement of the tongue, palate, pharynx and larynx. The characteristic feature of the speech disorder here consists of complete recovery of articulation of words after a sufficient rest. Not only the muscles which serve for phonation, but also the muscles of the eyes, of the face, of the trunk and of the limbs are similarly affected. In all we observe the above-mentioned characteristic. Muscular atrophy is absent. There is a special electrical reaction in the affected muscles (myasthenic reaction) which consists of rapid exhaustion of muscular contractility.

7. *Apoplexy*.—Following an apoplectic insult, not infrequently is observed a heavy, difficult and indistinct speech apart from aphasia. The articulation of words is done with a more or less great effort.

8. *Parcisis*.—Dysarthria may appear at the onset of the disease. Here the speech is especially characteristic. Hesitation in pronouncing labial and guttural letters and mutilation of words are striking. However, the dysarthria is here only intermittent and transient in the beginning, but later it becomes continuous. Fatigue and emotion increase the dysarthria.

**Aphasia According to the Views of Pierre Marie.**—The classical ideas concerning the problem of aphasia have become a subject for reconsideration through the efforts of Pierre Marie. His contention is that the division of aphasia into a motor and sensory is no more tenable; that there is only one aphasia, namely, sensory aphasia, to which anarthria is sometimes added; that all aphasias present invariably an intellectual deficit which may vary from a simple slowness of normal functions to a total suppression of all the faculties; that the old Broca's aphasia is a mixed aphasia composed in various degrees of anarthria and of disturbances in the inner language. Anatomically, according to Marie, the third frontal convolution may or may not be found involved in cases of aphasia, but it plays no part whatever in the functions of language. The real lesion is found simultaneously in *Wernicke's zone* (see section on Aphasia) and in the *lenticular zone*, so designated by Marie. A brief review of the classical "zone of language" may be necessary for the proper appreciation of the change of view as advocated by Marie.

The "zone of language," as formerly understood, is placed along the fissure of Sylvius and includes the following portions: (1) Broca's region or the posterior portion of the third frontal convolution and the cortical tissue immediately adjacent to it; (2) Wernicke's region or the posterior portion of the first and second temporal convolution; (3) angular gyrus.

All these centers are placed in the left hemisphere in right-handed and in the right hemisphere in left-handed individuals.

To the language zone belong: (1) two series of association fibers, *short* and *long*, (2) special association fibers of the corpus callosum, and (3) projectile fibers. The *short association fibers* serve to unite two neighboring convolutions; to this group also belong the intracortical fibers which are found in the deep layers of the cortex. The long asso-

ciation fibers serve to connect various areas of the speech centers. They are: (a) the superior longitudinal bundle which connects Broca's region with Wernicke's region and the angular gyrus; (b) the inferior longitudinal bundle which connects the occipital lobe with the angular gyrus and temporal lobes; (c) the occipitotemporal bundle which connects the occipital lobe with the temporal and frontal lobes. The fibers of the corpus callosum play an important part in bringing in communication the bilateral cortical centers of the speech zone, so that Broca's region, Wernicke's zone and the angular gyrus of each hemisphere are respectively connected with the corresponding areas on the opposite side.

The *projection* fibers originating in the cortex of the speech centers reach the optic thalamus or, originating in the latter, terminate in those centers: (1) From Broca's area they pass through the anterior segment of the internal capsule and terminate in the anterior portion of the thalamus. (2) From Wernicke's zone they pass through the sublenticular portion of the internal capsule and end in the neutral parts of the thalamus and in the internal geniculate body. (3) From the angular gyrus they pass through the retrolenticular portion of the internal capsule and end in the pulvinar and the external nucleus of the thalamus.

MARIE'S CONCEPTION OF THE SPEECH ZONE.—According to him the speech area is localized in the so-called "lenticular zone." Under the latter term is designated a square area limited anteriorly by the white substance of the third frontal convolution, posteriorly by Wernicke's area, externally by the insula, internally by the wall of the third ventricle. The lenticular zone, therefore, comprises the external capsule, the lenticular and caudate nuclei, the anterior and posterior segments of the internal capsule, also the optic thalamus.

According to Marie, the lenticular zone plays an enormous rôle in phonation and in coördination of movements indispensable for articulated speech. He says that the lenticulostriated ganglia, either by themselves or through their afferent and efferent pathways, represent in the mechanism of language a body far more important from a motor standpoint than the cortical center of the old Broca view.

DISCUSSION.—The anatomy of the lenticular and caudate nuclei and particularly the study of secondary degenerations show that no fibers from these nuclei enter into the composition of the cerebral peduncles. If disturbances of speech occur in lesions of the lenticular nuclei, such lesions are always accompanied by lesions of the adjacent internal capsule. It is well known that an involvement of the knee and the adjacent portion of the posterior segment of the internal capsule gives disturbances of speech of a paralytic nature, namely, dysarthria. Dejerine has shown that through this portion of the internal capsule pass fibers coming from the operculum, which is the motor center for the lips, tongue and larynx. In the classical motor aphasia there is no paralysis of the organs involved in the mechanism of phonation and articulation. Here not only the spoken language is altered, but also the inner language. Such a patient has no spontaneity in bringing before him auditory images; the few words that he pronounces he utters

cortex of the ascending parietal, but the contrast between them and the intense alterations in the frontal is so great that one must conclude that the motor cortical centers belong exclusively to the ascending motor convolution. (Probst,<sup>24</sup> Campbell,<sup>25</sup> Rossi and Roussi<sup>26</sup> and Souques and Barbé.<sup>27</sup>)

The last argument in favor of the exclusive motor character of the precentral convolution is found in Flechsig's "Embryological Studies." Basing his argument on the process of myelinization, he demonstrated that the ascending frontal convolution possessed a motor type, and the ascending parietal a sensory type.

The motor character of the precentral convolution is readily recognized from the convulsive and paralytic symptoms produced by an irri-

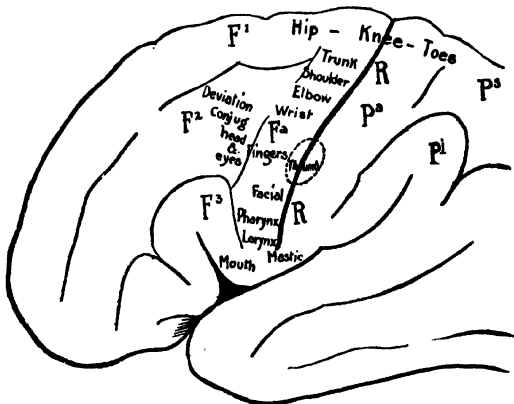


FIG. 4.—MOTOR CENTERS (after Lamacq).

(From Gordon's "Diseases of the Nervous System," P. Blakiston's Son & Co.)

tation or a destructive lesion of this area. The latter controls each individual muscle or group of muscles on the opposite side of the body. The upper fourth of the ascending frontal convolution and of the rolandic fissure, also the anterior portion of the paracentral lobule lying on the median surface, contain the motor center for the lower extremities. The two middle fourths of the same convolution represent the center for the upper extremities: from above downwards lie the centers for shoulder, arm, hand and fingers. The center for the muscles of the head lies in the lower fourth of the convolution and in the rolandic operculum. The center for the trunk lies between those of the extremities.

Clinical observation on focal epilepsy or electrical stimulation of the motor centers has shown that in each of the above areas exist secondary centers which correspond to the function of muscles of segments of the limbs. Thus there are centers for the shoulder, elbow, wrist, fingers,

thigh, knee, ankle, toes; for the head, individual centers control the movements of the face, tongue, lips, pharynx and larynx. The larynx has two centers—one for each of its two functions, viz., respiration (abduction of the vocal cords) and phonation (adduction of the vocal cords).

Each center controls muscular groups of the opposite side of the body and the reason of it lies in the decussation of the pyramidal fibers. There is, however, a certain group of muscles which are under the influence of centers of both hemispheres; in other words, some centers control simultaneously muscles of both halves of the body. Such bilateral centers exist for: (1) The muscles of the eye—elevation and lowering of both eye globes are produced simultaneously. (2) The orbicularis palpebrarum and frontalis muscles. The integrity of the upper portion of the facial nerve in organic facial palsy (*see Hemiplegia*) is also probably due to bilateral innervation of the upper part of the face. (3) The muscles of mastication. (4) Some muscles of the tongue. (5) Muscles of deglutition. (6) Muscles of the larynx. (7) Muscles of respiration and the diaphragm, and the intercostal muscles.

#### JACKSONIAN OR FOCAL EPILEPSY

**Etiology.**—Jacksonian epilepsy is almost always due to a focal cortical lesion which paroxysmally excites the motor area. At first there is a mechanical irritation of the cortex, but later an inflammatory condition develops. The irritation may be produced by tumors, hemorrhage, sclerosis, localized meningitis or meningo-encephalitis of syphilitic nature, hematoma or fragments of skull in traumata. There are also other conditions in which focal epilepsy has been observed, viz., intoxications, such as alcoholism and saturnism, also in uremia. Finally, peripheral irritation may sometimes be accompanied by jacksonian attacks, as, for example, cicatrices, polyps, burns or injury to nerve-trunks. A reflex origin is here the probable pathogenesis of the convulsive seizures.

**Symptomatology.**—Focal or partial epilepsy was first observed in hemiplegics on the paralyzed side by Bravais, but H. Jackson (1869) deserves credit of pointing out the relationship between unilateral convulsions and a cortical lesion in the motor area on the opposite side of the brain. The disorder consists of tonic and mainly of clonic convulsions, at first slight but gradually becoming more and more pronounced. They commence in a very limited area of a limb, such as a finger or a toe, and then progressively invade the neighboring parts—hand, forearm, arm, face, or from the toe to the leg and thigh.

**ONSET.**—According to the seat of the onset, focal epilepsy may be *facial*, *brachial* or *crural*. The knowledge of the seat of the onset is of major importance for therapeutic reasons, as it enables one to localize the lesion. If, for example, the convulsions appear first in the upper extremity, the lesion is in the middle portion of the ascending frontal convulsion on the opposite side. (*See preceding section for motor localizations.*)

In the *facial* form, the spasm affects the face and neck. Either one angle of the mouth is drawn up or one eye is rolled up; the head is turned toward the same side. The convulsions become precipitated and soon invade the muscles of the neck and of the arm. The forearm rapidly becomes pronated, the hand closes. Immediately the lower extremity becomes extended and rigid. The clonic contractions follow instantly.

In the *brachial* type, which is the most common, the initial symptom appears in the thumb, which becomes flexed and the other fingers follow. The hand is pronated, a rigid flexion of all the segments of the limb sets in and the convulsive movements begin immediately. The face and the lower extremity follow.

In the *crural* type the initial symptom appears in the great toe. Unlike the upper extremity, here the tonic contractures are rare, clonic movements appearing usually from the beginning. The upper extremity and the face become invaded subsequently. The order of appearance of the symptoms as just described is not always observed.

The convulsions may remain confined to the part in which they first appeared, but in the majority of cases they invade other parts of the same side. Sometimes they may become generalized and affect the opposite side. In the latter case, the importance of the knowledge of the onset of the convulsions cannot be overestimated. The seat of the first appearance of the muscular contractions is the most valuable "localizing sign." Surgical intervention is based almost exclusively upon this information.

**THE AURA.**—An attack is frequently preceded by an "aura" which may be motor, sensory or psychic. The motor aura consists of an involuntary movement in some of the muscles. The sensory aura may be a sharp, lightning pain, a tingling or a sensation of burning, or else a numbness in the part in which the convulsion is to appear first. The psychic aura consists of visual or auditory hallucinations (seeing a flash of light, or colored objects, hearing a sound, etc.). In some cases a state of confusion precedes an attack. Loss of consciousness is not constant. In the majority of cases, consciousness is preserved, especially when the convulsions remain focal. The patient witnesses then the entire cycle of symptoms. Loss of consciousness is observed invariably in those cases in which the convulsions become generalized and very frequently when the unilateral convulsions invade the face in their progressive course. Not uncommonly a jacksonian attack leaves a paralysis in the limbs involved, but the palsy is usually transitory, may last twenty-four or forty-eight hours, although sometimes it may remain permanent. In the latter case, there is probably a certain permanent damage of the cortical tissue (hemorrhage followed by softening). When the paralysis is transitory, no rigidity is observed in the limbs, but increased knee-jerk and sometimes Babinski's sign will be observed. The paradoxical reflex has been observed by the writer in every case and disappeared when the paralysis disappeared.

**VARIETIES OF ATTACK.**—A jacksonian attack may be *motor* and *sensory*. In the former, besides the typical seizure, in which clonic con-

vulsions follow the tonic ones, there is a form in which the entire attack consists exclusively of tonic contractions. In such cases the irritating lesion is in the subcortical tissue.

In the *sensory* variety, the entire attack consists of a sensory phenomenon. In a patient under the writer's observation there were brief attacks of coldness and numbness in the entire left side of the body. This lasted but two minutes, during which time she felt dazed; her face was pale and after the attack was over she went to sleep.

The War has supplied us with examples of jacksonian attacks in which the aura is in the sphere of special sensorium. Lereboullet and Mouzon<sup>28</sup> report a case of a soldier injured by a ball which penetrated the right occipital lobe. The jacksonian attacks which made their appearance about four weeks later were confined to the left side and were always preceded by an aura of visual hallucinations. The patient saw bizarre images, animals or objects without special colors; they were rather silhouettes. The hallucinations lasted as long as the patient's vision was more or less preserved. When later the patient became blind (cortical blindness), the hallucinatory aura disappeared. Visual hallucinations, therefore, in epilepsy may have a localizing value and indicate an irritation of the visual region.

*Epilepsy Following Cranial Traumatism.*—The following forms of jacksonian epilepsy have been observed in soldiers with cranial traumatism:

(1) Involuntary movements occurring in paroxysms between the jacksonian attacks. They affect a segment of the limb or the whole limb in which the convulsions occur. These movements consist of pronation or supination of the hand, flexion of the fingers or movement of opposition of the thumb.

(2) Paroxysmal tremor of one limb or of a half of the body preceding epileptic seizures or occurring after fatigue or emotion.

(3) Tremor with rapid oscillation affecting especially the distal end of the limb and increasing with muscular efforts and fatigue, but improving after rest.

(4) Clonic movements affecting one or several fingers, precisely those in which the epileptic seizures commence. The movements are: flexion of a finger, abduction, adduction or opposition of the thumb; the oscillations sometimes resemble those of paralysis agitans.

Cases are now on record where all these phenomena disappeared after operative procedures over the cortical areas of the opposite side. Such cases are those of Polosson, Collet, Parhon, Vasiliu and of others.<sup>29</sup>

*Jacksonian Paresis.*—There is another jacksonian variety to which Meigs and Bénisty<sup>30</sup> called attention, under the name of "jacksonian paresis." It consists of attacks of sudden and transitory paresis affecting the limb opposite the cranial injury, but more frequently both symmetrical limbs. In some cases there were also epileptic seizures in the same limbs. The paretic state was always accompanied by vasomotor disturbances, viz., cyanosis of the same limbs.

In discussing the pathogenesis of this condition, the authors express



this view, that because of a vascular disorder the motor and vasomotor disturbances are probably dependent on a disturbance of the intracranial sympathetic apparatus. The change of color of the face, changes of the pulse and respiratory rhythm in the seizures are all evidences of participation of the sympathetic system. It is therefore plausible to admit that the centers regulating the circulatory apparatus play a certain rôle in the jacksonian phenomena.

*Epilepsia Partialis Continua*.—In 1894 a special form of partial epilepsy was described by Kojevnikoff under the name of *epilepsia partialis continua*. It is characterized by the coexistence of typical epileptic seizures of the generalized or jacksonian variety and persistent involuntary contraction of muscular groups between the seizures.

The intervallary muscular contractions are clonic and their range varies from fibrillary contractions to very wide movements; they always occur in the same part of the body; they are more violent immediately before the typical seizures; they cannot be controlled by the will; they increase upon emotion; they interfere with locomotion as the power of the affected muscles is diminished; atrophy of the latter is occasionally observed.

The very few pathological records in the literature show that the condition may be due to a localized lesion in the motor cortex. (Cases of Osokin<sup>31</sup> and Krumholz.<sup>32</sup>) Choroschko incriminates also the optic thalamus and the posterior quadrigeminal bodies.

**Prognosis**.—The *prognosis* depends upon the lesion. If the matter is removable, such as an encapsulated tumor, the outlook is favorable. It is also favorable in syphilitic cases.

In the majority of cases the continuous irritation of the cortex leads to its destruction, so that eventually paralysis develops on the affected side.

**Treatment of Focal Epilepsy**.—Medical treatment is indicated only in cases in which the etiologic factor is intoxication, uremia, or syphilis. **Antisyphilitic medication** should be administered in all operative cases before surgical intervention is decided upon. A trial of **mercury**, **iodids** and **arsphenamin** is always justifiable.

As to **operative procedures**, a careful mapping out of the area involved, aided by *x-ray* pictures, is a necessary precaution (*see* Localizations). Kocher believes that the high pressure of the cerebrospinal fluid is the cause of epilepsy. He therefore removes a small round piece from the skull, excises the dura, replaces the bone and covers it with the incised integument.

Horsley determines first the seat of "signal center" by stimulating the supposed area with a very weak faradic current. When a motor manifestation is reproduced, he excises the area even if there is no evident local lesion.

Krause also takes as a guide the signal center and removes 20-25 mm. of cortical surface and 5-8 mm. in depth. The paralysis that may follow the operation is only transitory if the dimensions of the excised area are not increased above the figures given by Krause. Horsley's method has been used with satisfaction in the *epilepsia partialis continua*.

### III. POST-ROLANDIC AREA

#### (*Ascending Parietal Convolution*)

In the preceding section clinical, experimental, histological and embryological evidences were presented in favor of a purely sensory function of the postcentral gyrus. As an additional corroboration may be mentioned a recent experimental contribution of Van Valkenburg<sup>33</sup> on sensory localization of the cortex. On two patients suffering from jacksonian epilepsy he performed craniectomies. The first stage of the operation was done under general anesthesia. The second stage was done a few days later under local anesthesia. Electrical stimulation during the latter of the postcentral gyrus evoked in the patient paresthesia and as the operator moved the electrodes upwards or downwards the subjective sensations of pricking, tingling, pins and needles appeared in the corresponding parts of the limbs or face. These cortical centers were opposite to and on the same horizontal level as the corresponding motor centers on the precentral gyrus. The division of the latter into several centers is totally applicable to the postcentral gyrus (*see* Motor Area).

If the question of sensory function of the postcentral convolution appears to be definitely settled, the problem of distribution of different forms of sensibility in the cortex is still a matter of debate. Available evidence at present goes to suggest that there is a dissociation of sensibility in cortical lesions, and that touch, muscle sense, discrimination of compass points, stereognosis and appreciation of warm and cool temperatures are apt to be lost, while pain and deep pressure may be preserved. There is also evidence to indicate that the segmentation of the skin of the body as represented in the spinal cord is also represented in the cerebral cortex.

### IV. PARIETAL LOBE PROPER

In discussing sensory localization in the cerebrum, one must consider not only the ascending parietal convolution but also the *parietal lobe proper*.

The parietal lobe presents three distinct portions: superior parietal lobule, supramarginal lobule, and angular gyrus.

For a long time the parietal lobe was considered as a part of the sensory zone, but the work, especially of Dejerine, showed that the entire parietal lobe does not necessarily participate in causation of hemianesthesia. For Nothnagel and Bruns the superior parietal lobule controls tactile and stereognostic senses, also the sense of position. Redlich and von Monakow consider the supramarginal gyrus as the center of muscular sense and of the sense of position. The angular gyrus is admitted by all observers as the center of word-seeing. (*See* section on Aphasia.)

Although our knowledge concerning separate localizations for each form of sensations is not definite, nevertheless it is fairly well established that the superior parietal lobule together with the ascending parietal convolution can be considered as the cortical center for general sensibility. An irritative lesion in this area will cause jacksonian epilepsy with a sensory aura.

#### DISTURBANCES OF STEREOGNOSIS

In the same area is also placed the *stereognostic* sense by the majority of competent observers. Under this term, generally speaking, is understood the faculty of recognizing the form, size and consistency of objects by touch. Inability to recognize the characteristics of the objects is called "astereognosis." Although various other sensibilities besides touch participate in the perception of an object, such as muscular sense, temperature, weight and pressure, nevertheless astereognosis has been observed in cases in which all other sensations were found intact. Stereognosis must be considered as a special sense which has a special cortical center. The latter has often been found to be the superior parietal lobule. (Mills, Burr, Starr and others.) However, it should be borne in mind that this is not the exclusive seat of the stereognostic sense. For example, in lesions of the motor area astereognosis has been noted. On the other hand, in lesions of the parietal lobe, the stereognostic sense has been found intact. In one of the author's cases<sup>34</sup> a bullet entered the left parietal region and subsequent operative procedures lacerated very extensively the superior parietal lobule without involving the stereognostic sense.

The term "stereognosis" requires further elaboration. In the process of recognition of an object a discrimination should be made between its form or shape and its nature. These two different functions have been frequently confounded and described under one name—"stereognosis." Close observation reveals the fact that in certain cases one faculty may exist without the other, that the knowledge of the form of an object does not constitute the knowledge of its nature. The latter is a complicated perception of a higher order, and has been aptly called "symbolia" (*Claparède*). Astereognosis, therefore, is an inability to recognize the form; and asymbolia an inability to understand the nature of an object and to name it.

The contention has been that the recognition of form and nature of an object is dependent upon the integrity of all elementary sensibilities, such as touch, pain, temperature, pressure, movements, posture, etc. *A priori* one must concede that a perception of a high intellectual order such as form and nature of objects is the result of association of all individual senses. But when one attempts to analyze carefully the cases that come under observation, one finds that this contention cannot be maintained. There are cases in which gross changes in the deep and superficial sensations existed together with asymbolia; there are others in which asymbolia was absent, and still others in which asymbolia co-

incided with extremely slight changes in other sensations. Neither the stereognostic perception nor the faculty of recognizing the nature of objects (*symbolia*) is always dependent upon other forms of sensations. Stereognosis and *symbolia* are independent phenomena; their relation to the elementary sensation is meager; they consist of complex associative processes of the highest order, in which the other well-known sensibilities play a minor rôle. (Cases of Raymond and Egger,<sup>35</sup> Rose and Egger,<sup>36</sup> and A. Gordon.<sup>37</sup>)

A very important section concerning the function of the left parietal lobe is that relating to the phenomena of *apraxia*. This subject will be discussed in the section on *Corpus Callosum*.

#### SENSORY DISTURBANCES OF CEREBRAL ORIGIN: HEMI-ANESTHESIA

**Characteristics of Hemianesthesia.**—When the parietal region is involved, there will be present a *hemianesthesia* of the half of the body on the opposite side, including the mucous membranes of the head cavities. The disturbance will be observed in the superficial and deep sensibilities and is more marked in the upper than in the lower extremity, trunk and face. It may affect only one extremity. The characteristic feature of cerebral hemianesthesia lies in the fact that the distal portions are more affected than the proximal ones: the hand, for example, is more anesthetic than the forearm, the foot more than the leg. The reversed order is observed during the process of improvement: the return of sensory function, which is a slow process, commences in the proximal parts and advances towards the periphery, so that in the hand, for example, the sensations return last. The intensity of hemianesthesia varies. As a rule, it is pronounced at the beginning but it gradually subsides. It is very rarely complete and total. It is usually more persistent in extensive than in small lesions, in aged than in young individuals.

**Dissociation of Superficial and Deep Sensations.**—It was mentioned before that frequently all forms of sensation are simultaneously involved. Sometimes, however, a dissociation of the superficial and deep sensibilities is observed. Thus, touch, pain and temperature may be but slightly disturbed, and the deep sensations, such as position, muscular and stereognostic senses, are totally abolished or greatly impaired. In some cases there may be a dissociation within each of these groups of sensations: one form may be totally abolished, while the others are intensely pronounced, etc. Generally speaking, in hemianesthesia of cerebral origin the deep sensibilities are usually more pronounced than the superficial ones, viz., stereognostic, muscular, localizing and osseous forms of sensations. When the involvement of the deep sensibilities is intense, there will be present a disturbance of motor coördination, as the patient is unable to use his anesthetic limbs.

**Cortical Sensory Syndrome.**—Dejerine, basing himself upon a large number of observations of other writers and especially upon his personal investigations, isolated a symptom-group to which he gave the name of "cortical sensory syndrome." The sensory disturbances of this

syndrome are quite constant and observations gathered during the War, when injuries occurred with strict localization to the parietal area, proved it to be quite accurate. The symptoms are: (a) Profound changes in the sense of position (active and passive), in the sense of localization, in the recognition of the points of compass, and in the stereognostic sense. (b) Very slight changes or no changes at all are observed in the sensibilities of touch, pain and temperature, also in deep pressure and in the osseous sensations as exhibited in the test with the tuning fork.

Among all the cases concerning this sensory syndrome, the following three deserve special mention. One is described by G. Guillain<sup>38</sup> in 1918: A soldier was injured, during an attack by the enemy, in the upper and middle portions of the ascending parietal lobe and in the anterior portion of the superior parietal lobule. The sensory disturbances were as follows: (1) no spontaneous pain; (2) preservation of tactile sense; (3) very light hypo-algesia of the arm, trunk, leg on the opposite side, but not of the neck and face; (4) integrity of temperature sense; (5) loss of vibratory sensibility; (6) loss of sense of position in the wrist and fingers; (7) absolute astereognosis. There was no hemiplegia nor aphasia. The two other cases taken also from the war records were described by G. Roussy and J. Branche<sup>39</sup> in 1918. In both there was an injury in the parietal region and the sensory disturbances were similar to those of Guillain's case, but confined exclusively to the hand on the opposite side.

**Topographical Distribution of Hemianesthesia.**—The topographical distribution of the cerebral hemianesthesia presents sometimes certain peculiarities. From 1906 it has been observed that in some cases the anesthesia instead of being segmentary was radicular, resembling therefore the radicular distribution of spinal origin. Thus, in addition to the hemianesthesia of the cortical variety, there were also longitudinal bandlike anesthetics on the internal or external side of upper or lower extremity. Recently Dejerine and Mouzon,<sup>40</sup> also André-Thomas,<sup>41</sup> reported such cases from the war records. Whether such occurrence is due to increase of pressure in the spinal canal thus compressing the spinal roots, or there are special cortical areas in the brain which are capable of producing a radicular sensory distribution similar to those of the spinal cord, it is impossible at present to determine accurately. The differential diagnosis between cortical and capsular hemianesthetics will be discussed in the section on The Internal Capsule.

## V. OCCIPITAL LOBE: HEMIANOPSIA

**Anatomical Considerations.**—The function of the occipital lobe is chiefly concerned with *vision*. Among the first experiments on the occipital lobe were those of Munk.<sup>42</sup> He observed that a lesion of one occipital lobe produced a *homonymous hemianopsia* toward the opposite side, viz., a more or less complete blindness of the *homonymous* halves

of each of the visual fields. The term "right hemianopsia," for example, means that the right half of each visual field is blind. Further experiments of Munk and Loeb, and especially of Luciani,<sup>48</sup> have shown that although each visual sphere is chiefly in relation with the opposite eye, it is also in relation with the outer quadrant of the eye on the same

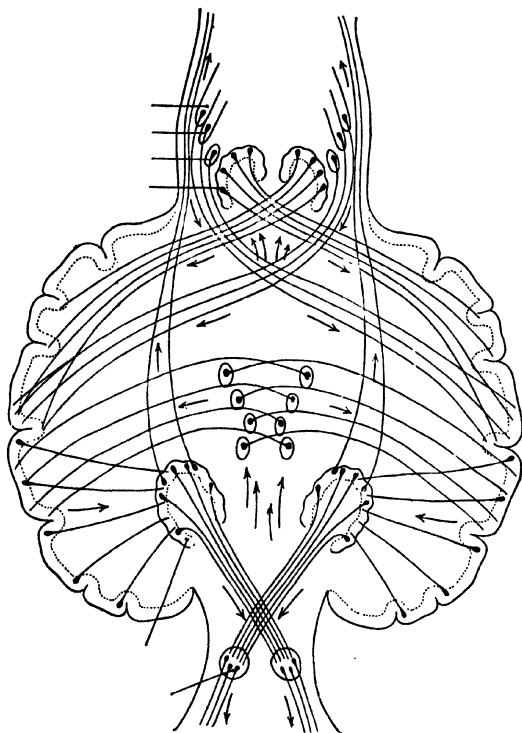


FIG. 5.—OPTIC CENTERS AND TRACTS.

(From Gordon's "Diseases of the Nervous System," P. Blakiston's Son & Co.)

side, so that destruction of the visual center in one hemisphere paralyzes the inner three-fourths of the opposite retina and the outer fourth of the eye on the same side. Monakow<sup>44</sup> observed that destruction of the occipital region led to atrophy of the left external geniculate body, left anterior quadrigeminal body, left optic tract and to some extent to atrophy of the right optic nerve. This important observation was corroborated by many investigators. (Sharkey, Gudden, Ganser, Ferrier, etc.)

Anatomically the visual area of the occipital cortex is an expansion of the optic radiations. The latter, passing through the retrolenticular segment of the internal capsule, connect the cortical visual center with the primary optic centers. The study of degenerative lesions in the visual cortex permits the tracing of the entire visual pathway as follows: The optic fibers of the retina aggregate as the optic nerve and further back separate at the level of the chiasma. The largest number of these which represent the nasal half of the retina decussate in the median line of the chiasma with similar fibers coming from the opposite eye. The smaller bundle of the optic fibers remains on the external side of the chiasma. Each optic tract, therefore, behind the chiasma consists of a larger bundle containing all the fibers of the nasal retina of the opposite eye, and of a smaller bundle containing the temporal fibers of the same eye. Further back each optic tract comes in relation with the primary optic centers, namely, the anterior quadrigeminal body, external geniculate body and the postero-external portion of the pulvinar. From these centers a system of fibers (optic radiations) is directed around the occipital portion of the lateral ventricle to the occipital lobe and especially to the cuneus, calcarine fissure on the mesial surface and the lingual and fusiform lobules. Thus it is explained why a lesion in the occipital lobe, as well as of the optic radiations or of the optic tracts, will produce homonymous hemianopsia.

The anatomical pathway just traced shows that the relation of each optic tract with the occipital cortex is homolateral, viz., with the cortex of the same side; also that the fibers emanating from identical points of both retinae terminate in the cortex alongside of each other, so that a lesion which will destroy one will necessarily destroy the other. As to the hemianopsia with relation to the side of the lesion, it should be borne in mind that the lesion is crossed with regard to the visual field.

**Characteristics of Hemianopsia.**—From the preceding discussion it is evident that hemianopsia is a symptom but not the lesion itself. It is a more or less complete blindness of one half of the visual fields due to an anesthesia or paralysis of the retina of the opposite side. It is called *homonymous* when the corresponding halves of both retinae are affected; it may be then right or left, superior or inferior. When the blindness of the visual field occurs in one half of one eye and in the opposite half of the other eye, the hemianopsia is then *heteronymous*: it is *nasal* when the right half of the left and the left half of the right visual fields are blind; it is *temporal* when the right half of the right and the left half of the left visual fields are blind; as for example, in lesions situated in the anterior or posterior angle of the chiasma.

Hemianopsia may be complete or incomplete. In the *complete* cases Bard observed loss of palpebral reflex (winking) when an object is suddenly placed in front of and close to the blind half of the visual field. In the *incomplete* variety the blind side may perceive the form of an object but not the color; it is then a case of *hemiachromatopsia*. Hemianopsia may be *double* when the cortical lesion is bilateral.

**HOMONYMOUS HEMIANOPSIA** has this special characteristic feature, that the *central vision* is always preserved, so that hemianopsic eyes have a normal acuity of vision and the patient frequently ignores his hemianopsia. The reason for it lies in the fact that the macula of each eye is in anatomical relation with both optic tracts and both cortical centers by means of a direct and crossed bundle of fibers, so that even in double hemianopsia central vision has been reported to be normal. Such were the cases of Förster<sup>45</sup> and of Beever and Collier.<sup>46</sup> In order that a lesion, for example, of the right optic tract or of the right cortical center leave the central vision of both eyes intact, it is necessary that the bundle of fibers passing from the right eye remain connected with the normal left cortical center by means of a crossed bundle, and that the left macular bundle remain connected with the left cortical center by means of a direct bundle. Each macula is, therefore, in relation with both hemispheres and each optic tract contains a macular bundle from the same eye and from the opposite eye.

**CROSSED HEMIANOPSIA**, therefore, is caused by a lesion on the pathway between the optic tracts at their origin in the chiasma and the occipital cortex. According to the seat of the lesion on this long pathway there will be present special symptoms in addition to the hemianopsia. The knowledge of these special symptoms will enable one to localize the lesion:

(a) The pupillary fibers of the optic nerve go through the anterior quadrigeminal body. From the latter a system of fibers connect the former with the nucleus of the third nerve which controls the pupillary sphincter and which is located in the gray matter of the aqueduct of Sylvius. A lesion, therefore, in front of the quadrigeminal bodies will interrupt the connection between the pupillary fibers of the optic nerve with the nucleus of the sphincter of the pupil. An injury at this level of the optic tract will give place to a homonymous hemianopsia with no response of the pupil when a light is thrown into the latter on the blind side of the visual field. A lesion placed posteriorly to the quadrigeminal bodies will not interfere with the pupillary reaction. The inaction of the pupil under the circumstances just described is known under the name of "hemianopsic pupillary reaction" or "Wernicke's pupil."

One must not infer, however, that a hemianopsic pupil will be observed in lesions of any one portion of the entire pathway between the primary optic centers (anterior quadrigeminal bodies, etc.) and the retina. It has been found wanting in lesions of the chiasma, in partial embolism of the central retinal artery, but in all, hemianopsia was present.

The other special symptoms observed in hemianopsia from lesions of the optic tracts near the primary optic centers are: (1) ocular palsies because of the proximity of the oculomotor nerves where the tracts embrace the cerebral peduncle; (2) crossed hemiplegia because of the presence of the crura at this level; (3) gradually developing atrophy



of the papilla (more pronounced in the opposite eye) because of the descending degeneration originating in the affected optic tract.

(b) In lesions of the primary optic centers (anterior quadrigeminal bodies, external geniculate body, pulvinar) homonymous hemianopsia has rarely been observed. Henschen calls attention to hemorrhages in the pulvinar, which in his opinion may produce a hemianopsia of the inferior quadrants through compression of the external geniculate body. Finally, in lesions of the primary optic centers there will be present also a hemianesthesia with or without hemiplegia, according to whether the posterior limb of the internal capsule is involved or not.

(c) In cortical hemianopsia there will frequently be present hemiplegia and hemianesthesia on the side of the hemianopsia because the destructive lesion in the occipital lobe and optic radiation frequently extends to the internal capsule and optic thalamus. In cases of right cortical or subcortical hemianopsia, the angular gyrus is frequently involved; the result is word-blindness in addition to the hemianopsia. In such cases the papilla is found to be normal and there is no Wernicke's pupillary reaction.

Von Monakow observed that in lesions of the superior border of the calcarine fissure and of the cuneus there is atrophy of the anterior portion of the external geniculate body; clinically there will be a homonymous hemianopsia of the inferior quadrant according to Beever and Collier. When the inferior border of the calcarine fissure, also the lingual and fusiform lobules, is involved, the ventrolateral portion of the external geniculate body will undergo atrophy and the resulting homonymous hemianopsia will be evident in the superior quadrant. Practically the same conclusions were reached by Funkhouser<sup>47</sup> in a recent contribution: "Through destruction of the dorsal lip of the calcarine fissure and of the cuneus, the dorsal part of optic radiations and the dorsal part of lateral fibers of corpus geniculatum externum degenerate secondarily; secondary degeneration of the ventral part of optic radiation and of the lateral part of the corpus geniculatum externum takes place after a lesion of the ventral lip of calcarine fissure and lobus lingualis." All these anatomical facts prove that the corpus geniculatum externum is projected in the calcarine fissure. Minkowski's experimental researches on dogs indicate that the anatomical visual sphere is covered with a cyto-architectonic area and lasting visual trouble can be caused only by extirpation of the *area striata* which, as shown by K. Broadmann,<sup>48</sup> consists of a special calcarine type of cells. Its total extirpation produces a maximal visual disturbance, while extirpation of the convexity of the occipital lobes has, as a consequence, no or only a short or quickly passing restriction of visual fields if it remains confined to the cortex and does not affect the optic radiations.

To sum up the study of hemianopsia, one can say that it is caused by a lesion (tumors, softening, etc.) of the visual pathway between the chiasma and the occipital cortex. The special symptoms outlined above in sections *a*, *b* and *c* are so characteristic of the various areas of that

visual pathway that they will render considerable aid in the localization of the lesions. Their diagnostic value must not be overlooked.

In considering lesions of the optic nerve in front of the chiasma, one must bear in mind their anatomical arrangement (*see above*): in such cases hemianopsia may be *monocular* when only a half of one optic nerve is involved.

**CORTICAL BLINDNESS.**—*Double* hemianopsia means total blindness. As it is usually due to a bilateral cortical lesion, the subject will be discussed under the heading of Cortical Blindness.

The chief characteristics are: The visual fields are in the majority of cases reduced to an extremely narrow area in the center; the fundus oculi is normal and the pupillary reflexes are preserved. The central vision is therefore intact. If, as it usually happens, the central vision is at first lost, it has a tendency to return in a comparatively short time. This apparently paradoxical phenomenon, in view of a bilaterality of the lesion of the occipital lobe, finds its explanation in anatomical considerations. If the central vision remains intact, or it is rapidly re-established, while the rest of the visual field remains lost, it is to be presumed that a small area of the supposed macular center in the cortex had either escaped the original cortical lesion, or else there is no special center for the macula, but on the contrary the macula is in anatomical relation with the entire cortical visual zone. In the latter case it is conceivable that in the entire cortical area over which the optic radiations are projected one or another or several points corresponding to the macula remain intact. Indeed, the investigations, especially of von Monakow and Dejerine, show that the macular fibers, which form a distinct bundle in the optic nerve, terminate in a large number of cells of the external geniculate body and thus are brought into close relation with a very large number of optic radiations originating in those cells. Hence the macular fibers are projected over a large area in the cortical visual zone. In fact, the visual bundle emanating from the external geniculate body has been found to terminate in the cuneus, calcarine fissure, lingual lobe. This view, although based on anatomical facts, finds its corroboration in the clinical observations according to which a central scotoma of cortical origin has never been seen. Consequently the existence of a special macular center in the cortex cannot be admitted. Such is the view held by Dejerine. Nevertheless the last word on the latter has not yet been spoken. The War has furnished us with great varieties of lesions in the domain of the cerebrum. Among the latest information obtained from that source are those collected by A. Monbrun.<sup>49</sup> After a critical analysis of all records concerning the visual cortical center, he arrives at the conclusion that there is a macular cortical center which he places in the most posterior portion of the calcarine fissure. A similar view is held by Henschen, P. Marie, Chatelin. In another recent observation from the war zone, Souques and Ch. Odier express the opinion that there is a circumscribed cortical center for the macula and they localize it in the posterior portion of the occipital lobe.

## VI. TEMPOROSPHEOIDAL LOBE

In the course of his experiments for cerebral localizations, Ferrier<sup>50</sup> observed that when the superior temporosphenoïdal convolution was damaged on one side there was absence of the usual reaction to auditory stimuli on the same side. When the lesion was bilateral there was total absence of response to auditory stimuli. In one animal the superior temporosphenoïdal convolution was cauterized in both hemispheres. The animal (monkey) was allowed to survive for more than a year, during which time it enjoyed perfect health and the full capacity of all its faculties and powers with the single exception of hearing. Ferrier had also shown in at least a dozen cases in which he produced the most extensive lesions in the temporosphenoïdal lobe with the exception of its superior convolution, on one or both sides, that there were present clear signs of perception of auditory stimuli indicated by twitching of the ear and turning to the source of slight sounds, such as tapping, scratching or whispering close to the ear. Horsley and Schäfer had fully confirmed the results obtained by Ferrier.

Thus it was established that the superior temporosphenoïdal lobe is the cortical center of hearing. Flechsig, Monakow and Bechterew have shown that the posterior quadrigeminal and the internal geniculate bodies are in relation with the cortex of the temporal lobe and therefore with the auditory area. The fibers passing to these bodies originate in the ventral nucleus of the cochlear nerve and in the dorsal nucleus; they pass for the most part in the trapezoid body, partly to the lateral fillet on the opposite side and end in the internal geniculate ganglion. From the latter, fibers pass to the cortex of the temporal lobe, especially to the middle portion of the first convolution (Dejerine). Because of the existence, especially, of a commissure between the bilateral nuclei of the lateral fillet, each cochlear nerve is connected with both internal geniculate bodies, hence with both hemispheres. Consequently general audition is controlled by bilateral centers. Broadbent observed a case of a deaf-mute in whom atrophy of both superior temporal gyri was found. Mills describes a case of a woman deaf for thirty years in whom both superior temporal gyri were atrophied.

While the function of hearing in general is controlled, as we have seen, by bilateral centers, the special auditory function of "word-hearing" is associated only with one hemisphere, viz., with the left in right-handed and with the right in left-handed individuals. Word-deafness is a symptom of sensory aphasia and it is observed either in ordinary sensory aphasia with alteration of the inner language or as an isolated symptom with integrity of the inner language. It is necessarily connected with the hearing in general, as patients affected with word-deafness are not deaf, generally speaking. It is due to a lesion in the posterior third of the first (and perhaps of the second) temporal convolution. (For a detailed discussion of this subject see section on Sensory Aphasia.)

Some writers believe that the lower extremity and the apex of the temporosphenoidal lobe contain the centers for taste and smell. Ferrier, for example, observed impairment of these senses in his experimental work on higher animals (anosmia). He is of the opinion that in the case of impairment of both smell and taste following cranial injuries there is concussion and contusion of the lower extremities of the temporosphenoidal lobes where the olfactory and the gustatory centers are situated. But this view is not at all held by the majority of observers who place the gustatory and olfactory centers in the hippocampus and cornu ammonis.

## VII. MESIAL SURFACE OF THE HEMISPHERE

Some of the structures on the mesial surface have been already considered. Thus the paracentral lobule was discussed in the section on the Motor Area; the cuneus and the calcarine fissure in the section on the Occipital Lobe. On the following pages will be studied the

### HIPPOCAMPAL REGION

Ferrier,<sup>51</sup> from a series of experiments on animals, concludes that affections of *smell* and *taste* are related to lesions of the hippocampal lobule and the neighboring tissue. Munk also considers the hippocampal gyrus as the center of smell from the facts he observed in a case of a dog which had been rendered blind by bilateral lesion of its occipital region. This animal seemed to be unable, like other dogs, to detect by smell pieces of meat laid before it. After death, it was found that the hippocampal gyri had been, secondarily, almost entirely converted into cysts distended with fluid. This case is evidently a confirmation of Ferrier's experimental observations in favor of the localization of the olfactory centers in the hippocampal lobules. The cases of W. Ogle,<sup>52</sup> of Fletcher and Ransome,<sup>53</sup> also of H. Jackson,<sup>54</sup> all lead to the view that anosmia is due to softening in the hippocampal region.

If we refer to Embryology and Comparative Anatomy concerning the olfactory apparatus, we can see its close relationship to the hippocampal area. The olfactory nerves spring from the olfactory bulbs which lie on the cribriform plates of the ethmoid bone. The olfactory tract is joined to the hemisphere by two apparent roots, an inner and an outer root, separated by a triangular interval in the anterior perforated space (trigonum olfactorium). The inner root joins the mesial aspect of the anterior extremity of the gyrus fornicatus, while the outer root passes outwards across the sylvian fossa, where it fuses with the anterior extremity of the hippocampal gyrus. According to Broca,<sup>55</sup> the entire limbic lobe, which includes the callosal convolution, the hippocampus and cornu ammonis, constitutes the cortical olfactory zone. The trigonum olfactorium establishes the connections between this cortical

center, mamillary tubercles, thalamus opticus and the tegmentum of the peduncular region.

The histological researches of Campbell<sup>20</sup> suggest that the lobus pyramiformis, which consists of the external root of the olfactory lobe and of the gyrus hippocampus, must be considered as the principal cortical center of the olfactory sense. Finally Zuckerkandl's observation is quite significant. He found that animals with a highly developed sense of smell possess a large limbic lobe; the latter is atrophied in animals whose olfactory sense is rudimentary or absent. As to the individual rôle of each hippocampus, the researches of Gudden and Ganser<sup>56</sup> have shown that all connections of the olfactory tract are with the hemisphere of the same side.

In the determination of a cortical center of the sense of *taste* investigators met with considerable difficulties. Ferrier in his experimental work on animals had not succeeded in differentiating a special region relating to this faculty, but that it is in close relation with the olfactory center is probable. He believes that many of the cases of so-called loss of taste and smell are merely cases of loss of smell only, the impairment of taste extending only to the perception of flavors, which, as is well known, are compounded of taste and smell together.

The nerve of taste is the glossopharyngeal. Originating in the cells of the petrous and jugular ganglia, its fibers terminate in the upper half of the nucleus of the solitary bundle in the medulla. At the same level ends also the chorda tympani, the function of which is likewise partially gustatory. In their cerebral course they are all lost among the fibers of general sensibility, according to Dejerine, but Ferrier, as mentioned above, connects them with the lingual lobe in the olfactory center.

In connection with smell and taste, the observation of H. Jackson must be mentioned. In 1876, he described attacks consisting of a "dreamy state" preceded by peculiar sensations of taste and smell. During the attack the patient has a feeling of unreality and he recalls events that happened long ago. At the same time he keeps on moving his mouth and jaws as if he were chewing. These seizures are called "uncinate fits" and are observed in tumors of the tip of the temporo-sphenoidal lobe. Buzzard, in 1905,<sup>57</sup> reported similar cases in which lesions were found in temporosphenoidal lobes.

The above described facts of embryology, comparative anatomy and experimental physiology, also the few anatomicoclinical records, all speak strongly in favor of the hippocampal zone as being the cortical center of smell and taste. Nevertheless absolute and incontrovertible proofs of this contention are wanting. If one only considers the enormous difficulty in testing the sensibility to odors in lower animals, as distinguished from mere irritants of the schneiderian membrane, also if one will realize the practical impossibility of establishing lesions in the hippocampal lobe without injury to neighboring regions, the reason for hesitation in accepting the above view as final will thus be explained.

## VIII. BASAL GANGLIA

(*Optic Thalamus, Corpora Striata, Red Nucleus, Corpora Quadrigemina*)

Experimental investigation of the functions of the basal ganglia is surrounded with special difficulties. To reach them it necessarily involves injury to parts surrounding them and to the cortex. Hence one must largely depend on clinical observations for conclusions regarding

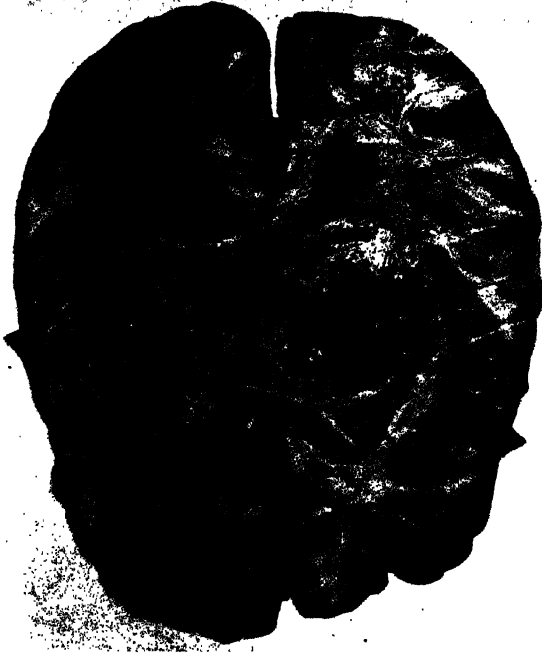


FIG. 6.—TUMOR IN LEFT BASAL GANGLIA.  
(Gordon, Courtesy *Archives of Internal Medicine*.)

lesions of basal ganglia. Nevertheless, for purposes of electrical stimulation, the basal ganglia can be reached by division of the corpus callosum.

The functions of the basal ganglia are still debatable in spite of a large number of accumulated anatomical, physiological and experimental data. It is known that the greater portion of the lemniscus, which is connected especially with the corpus striatum, degenerates in

a centrifugal direction; this is an indication, therefore, of the corpus striatum possessing a motor function. The connections of the optic thalami are with the longitudinal tracts of the tegmentum and the cortex and the function of the optic thalami is supposed to be chiefly sensory. An analysis of various clinical and experimental data with regard to the effect of destruction of the basal ganglia leads to the conclusion that neither motor nor sensory disturbances are permanently present if the fibers of the adjacent internal capsule are not damaged at the same time. In spite of this important dependence on the internal capsule, each of the individual basal ganglia possesses certain physiological characteristics which deserve special mention.

### THALAMUS OPTICUS

Luis and Fournié<sup>58</sup> intimated long ago that the optic thalamus was the ganglion of convergence of all the sensory tracts before they radiated into the cerebral cortex. Bechterew<sup>59</sup> found that, after destruction of the optic thalami in pigeons, rabbits and dogs, the animals were unable to express their feelings in the usual manner by cries or to make the mimetic movements characteristic of feeling or emotion.

It seems reasonably certain that the optic thalami are in close relation to the sensory tracts and centers: (a) the cutaneous sensory tracts of the internal capsule are in immediate relation to them; (b) the optic tracts are connected with the pulvinar; (c) through the pillars of the fornix the optic thalami are in relation with the cortical centers of smell and tactile sensibility; (d) through the corona radiata they are in relation with the occipitotemporal regions of the cortex which are sensory in function.

Monakow's experiments show that each nucleus of the optic thalamus is in relation to a definite cortical area and undergoes atrophy when this area is destroyed.

In 1903, Dejerine and Egger brought out a group of sensory symptoms which according to them has been so constant in cases with lesions of the optic thalami that the term "thalamic syndrome" was found by many writers to deserve a place in nosology of the nervous system. It was found that the thalamic syndrome was the result of a lesion in the external and internal nuclei, or in the pulvinar. The thalamus, being essentially a sensory organ connecting the periphery with the cortical centers by means of corticothalamic and thalamocortical fibers, a lesion of it would give place mainly to *hemianesthesia*.

**Symptoms.**—They are: *hemianesthesia*, *hemiataxia*, *hemiplegia*, choreiform movements, *athetosis*, pain on the anesthetic side. Sometimes *mimicry* is affected.

(a) *Hemianesthesia*.—It is pronounced for deep sensations, viz., muscular, tendinous, articular and osseous senses, position of limbs, the sense of active and passive movements of resistance, of force, of weight. *Astereognosis* is frequently present. The superficial sensations, viz., touch, pain and temperature, are but slightly involved. There is an

increased response to thermic or painful stimulations out of proportion to the intensity of the latter.

(b) *Hemiataxia* is slight and is dependent on the hemianesthesia.

(c) *Hemiplegia* is very slight. There is no contracture and the toe phenomenon is absent, although the knee-jerk is increased. It has a tendency to improve. Meynert, Schiff, Clarke and others observed in lesions of the thalamus: flexion of the arm on the opposite side, extension of the arm on the same side and head and eyes turned to the opposite side of the lesion.

(d) *Choreo-athetotic movements* in the anesthetic limbs are present, but not marked. They are brought out especially on voluntary movements.

(e) *Pain* on the anesthetic side is persistent, deep and sometimes paroxysmal, of a lancinating character. Instead of pain, there may be numbness, burning or tingling.

In addition to the above symptoms there may be *homonymous hemianopsia*, which indicates that the lesion is deeper and involves the visual fibers which originate in the pulvinar. *Taste, hearing* and *smell* are sometimes altered. *Trophic disturbances* and bladder involvement occur occasionally.

In a few cases of lesions of the thalamus, the following phenomenon was observed: on voluntary movements the muscles of the face contracted equally on both sides, but in the act of laughing or crying (emotional acts) the motion of the affected side was considerably diminished or else abolished.

For *differential diagnosis* between thalamic and cortical hemianesthesia see section on Parietal Lobe.

### CORPORA STRIATA

Nothnagel<sup>60</sup> in a series of experiments had shown that mechanical lesions limited to both caudate nuclei caused little, if any, interference with volitional movements. When both lenticular nuclei were destroyed the animals maintained their normal attitude but remained immovable and apathetic; they allowed their limbs to be placed in any position. Evidently destruction of the lenticular nuclei paralyzes the power of carrying desire into effect. Ferrier also observed that volition movements were paralyzed.

Comparing the function of the corpora striata with that of cortical motor centers, it was observed that both were centers of innervation of the same movements, but the corpora striata were of a lower grade of specialization. The innervation of the limbs as instruments of consciously discriminated acts is dependent on the cortical centers, while for purposes involving automatism or mere strength, the corpora striata are sufficient. The position of the corpus striatum in relation to the internal capsule naturally leads to a possible, if not inevitable, implication of the latter when a lesion is produced in the former, so that in a number of cases of motor paralysis it is difficult to entirely eliminate



the involvement of the tracts of the internal capsule. But more recent investigations make it very probable that the fibers of the internal capsule pass on to the cerebral cortex without entering into other relations with the basal ganglia than that of mere contiguity. The afferent and efferent fibers of the corpus striatum connect it with the optic thalamus and the subthalamic region, and there is no connection between the striatum and the cortex and the internal capsule. A few fibers perhaps cross the internal capsule to terminate in the thalamus. (Grünstein<sup>61</sup> and K. Wilson.<sup>62</sup>)

It is rather well established now that the corpus striatum could be considered as an independent motor center which is apt to produce motor manifestations without any participation of the neighboring internal capsule; also that among the constituents of the striatum, the lenticular nucleus is the part which controls those manifestations. As an additional evidence of the latter, Bechterew's experimental investigations<sup>63</sup> deserve special mention: He destroyed the motor zone and thus produced degeneration of the pyramidal bundle. By stimulating the caudate nucleus no effect was produced, but stimulation of the lenticular nucleus caused tonic muscular contractions on the opposite side.

In 1884, Meynert (*see* his text-book<sup>64</sup>) expressed the opinion that involuntary movements of athetotic or choreic character were due to an involvement of the corpus striatum. Tremor, resembling that of paralysis agitans, has been observed in lesions of corpora striata by Lewy.<sup>65</sup> Motor disturbances of paralysis agitans have been studied especially by Zingerle<sup>66</sup> and Förster.<sup>67</sup> They show convincingly that the hypertonicity is here of central origin in contradistinction to the hypertonicity of spastic paralysis in which it is manifestly influenced by peripheral stimuli. J. R. Hunt<sup>68</sup> justly calls attention to various phenomena of paralysis agitans which are in conformity with the experimental observations of Nothnagel, Ferrier and Bechterew (*see* above). He lays stress on the deficiency of the association movements in this affection: "Observe a case of paralysis agitans rising from a chair, with every indication of an extreme effort, and yet making no attempt to use the arms. Such a lack of coöperation on the part of the upper extremities would be very difficult to explain save as a grave disorder of the mechanism for the association of movements." . . . "If a case of advanced paralysis agitans is suddenly pushed over, the equilibrium is lost, but without the usual compensatory efforts on the part of the automatic and association motor mechanism. The loss of this mechanism explains the difficulty in initiating movements, the conspicuous inertia and the peculiar disturbances of the association of movements in habitual and more or less automatic acts."

Conspicuous atrophic changes in corpora striata have been found in cases of Huntington's chorea. (Alzheimer,<sup>69</sup> Kleist,<sup>70</sup> Marie and Lhermitte.<sup>71</sup>)

Double athetosis was also observed in affections of corpora striata by C. Vogt.<sup>72</sup> This writer found in addition also spastic contractures

and pseudobulbar paralysis, all of which symptoms she considers as a syndrome of the corpus striatum.

The next important contribution to the subject of the striatum symptom-group is that of S. A. K. Wilson.<sup>73</sup> He found a bilateral softening and progressive degeneration of the lenticular nucleus, chiefly of the putamen and slightly of the globus pallidus but without any involvement whatsoever of the internal capsule and pyramidal paths. Clinically the condition is characterized by a pronounced spasticity of the limbs and of the face without or with very little paralysis; by a bilateral tremor of all extremities of paralysis agitans type, which increases with voluntary movements; by a tendency to tonic and clonic spasms also athetoid movements; by dysphagia and dysarthria; by spasmodic laughing and crying (only occasionally); by absence of the toe phenomenon and preservation of the abdominal reflexes; finally by transitory mental disturbances; impairment of the capacity of retaining impressions, childishness, docility. As additional characteristics may be mentioned the familial nature of the disease and the presence of cirrhosis of the liver. The disease occurs between the ages of 10 and 25, in males more frequently than in females and it is very probably of toxic origin. The same observation was made by Gowers<sup>74</sup> but under a different title, viz., Tetanoid Chorea.

We are now in possession of quite a large number of cases all corroborating the findings of Wilson.

Ch. K. Mills<sup>75</sup> considers the subject of muscular tonicity mentioned above in connection with the corpus striatum by recognizing the existence of a tonectic apparatus which is structurally distinct from the pyramidal system and is extrapyramidal. He holds that the tone derived from a sensation and idea has a cortical localization in the mid-frontal and prefrontal regions (more highly developed in the right hemisphere) which by association tracts are connected with the corpora striata. Impulses are transmitted from the striothalamic system by way of cerebello-rubro-thalamo-cortical system to the pyramidal motor system. In this way the tone necessary to the steadying of synergic motor activity was acquired for normal movements. When this rhythmic tonectic influence was withdrawn by lesions of both lenticular nuclei for instance, the cortical tonectic centers, released from their striate connections, discharged directly by convolitional associating tracts on the cortical motor centers and thus arose the phenomena of hypertonicity. The tone in general is a cerebral cortical function and the three great elements represented in normal and abnormal movements are: the energy derived through the pyramidal apparatus, synergy from the cerebellum and tone through the cerebral tonectic apparatus.

The experimental, anatomical and clinical facts presented on the preceding pages establish in no uncertain terms the physiological relations of the corpus striatum. We have seen its important rôle in muscular tonicity, in muscular activity, in the causation of choreo-athetotic movements and of special tremors, also in other phenomena so characteristically found in Wilson's disease. The entire series of these phenomena

could be grouped under the name of "The Syndrome of the Corpus Striatum."

An analysis of the anatomicoclinical records concerning the corpora striata shows that their constituent portions have been variously involved: in some cases the authors speak of lesions in the corpus striatum, in others of lesions in the caudate nucleus, in still others of lesions in the lenticular nucleus. J. R. Hunt (loc. cit.) has collected all the facts accumulated in the literature and his own cases, and after a careful analysis attempts to establish from the anatomical standpoint two distinct syndromes, viz., *the syndrome of the globus pallidus* and *the syndrome of the neostriatum*.

Basing his argument on the histological structure of the striatum, he finds that the putamen is identical with the caudate nucleus (neostriatum) and they both are composed essentially of small pyramidal cells, among which are scattered very few larger cells. The globus pallidus (paleostriatum) is composed chiefly of large cells of the Betz motor type of the cortex. Besides, there is also a developmental difference between the two: the globus pallidus is much older, as its efferent system of fibers develops before that of the neostriatum and has an earlier myelinization. Thus Hunt draws a sharp line of distinction between the neostriatum, which consists of the nucleus caudatus and putamen, and of the paleostriatum, which is represented by the globus pallidus. The clinical manifestations due to lesions in each of the two portions of the striatum are equally distinguished by him. His conclusions are as follows: The corpus striatum is the infracortical center for the control and regulation of automatic and associated movements. The function of the neostriatum is inhibitory and coördinating, that of the paleostriatum is motor. A lesion of the former is followed by choreo-athetosis, a lesion of the latter by rigidity, tremor and disturbances of automatic and associative movements. A lesion affecting the large number of Betz type cells in the globus pallidus and the few cells of the same type in the neostriatum, or a lesion involving the large and small cells of either portion of the striatum, will give place to a combination of symptoms, such as observed in Vogt's or in Wilson's syndromes (see above). Hunt<sup>16</sup> considers the globus pallidus as the motor nucleus of the striatum and through its connection with the hypothalamic area, viz., nucleus ruber, corpus subthalamicum and locus niger, exercises a controlling influence upon the intersegmental nervous system through the medium of the extrapyramidal motor tract. The cells of the globus pallidus occupy therefore the same position in the extrapyramidal motor system as do the cells of Betz in the corticospinal system; the globus pallidus mechanism controls automatic and associated movements, whereas the higher cortical centers are concerned with isolated synergic movements. Moreover, the inhibitory effect upon the muscle tonus is also different in both mechanisms: a lesion of the pyramidal tract system is followed by the phenomena of spastic paralysis, while a lesion of the pallidal system is characterized by the phenomena of paralysis agitans.

As another important contribution to the function of the corpora

striata, and especially of the lenticular nucleus, must be mentioned the observation of Dana. He described a case of gas poisoning with a vasomotor (edema) and gangrenous condition of the skin. At autopsy a bilateral softening of the lenticular nucleus was found. (*Jour. of Nerv. and Ment. Dis.*, 1908.)

The preceding study of various motor phenomena observed in lesions of the corpora striata cannot be considered complete without some considerations concerning the *red nucleus*. It has been observed that in various pathological conditions of cerebral regions connected with the red nucleus, choreo-athetotic movements or posthemiplegic tremors were present. A question naturally arises: Is the red nucleus the center or else are its connections with all parts of the cerebrum the seat of these motor phenomena?

### THE RED NUCLEUS

The *red nucleus* was found in a state of degeneration in lesions of the following cerebral areas: prefrontal lobe, operculum and the mesial surface of the temporal lobe. The fibers originating in the frontal lobe reach the red nucleus through the anterior limb of the internal capsule and the subthalamic region. The fibers originating in the operculum go through the posterior limb of the internal capsule. The fibers from the mesial surface of the temporal lobe pass through the sublenticular segment of the internal capsule. (Monakow,<sup>77</sup> Archambault.<sup>78</sup>)

Besides its connection with the cortex, the red nucleus is also connected with the bulbar motor nuclei and the anterior cornua of the spinal cord. There are, therefore, two distinct associating pathways: (a) corticorubral and (b) rubrospinal. An analysis of the cases referable to an involvement of the red nucleus reveals the following facts and Archambault justly calls attention to this phenomenon of mimicry: In cases of involvement of the inferior facial nerve, the patient is unable to contract voluntarily the muscles innervated by this nerve, but he is able to do so when he laughs. Some authors have placed the center of mimicry in the thalamus. But the operculum, which sends out fibers to the red nucleus (*see above*), also contains the facial center. In normal conditions, the innervation of the facial muscles presupposes integrity of rubral as well as cortical connections of the nucleus of the origin of the seventh nerve. When the cortical connections are partly involved, which occurs in lesions of the thalamus in the vicinity of the red nucleus, automatism will take place. Moreover, the disturbed innervation of the inferior portion of the seventh nerve, which was observed in thalamic lesions, is usually transitory. Here is another argument against the existence of a mimicry center in the thalamus. Archambault further argues that spasmodic laughing and crying, which have been observed in lenticular and thalamic lesions, as well as in lesions of the tegmentum, are very likely the result of an irritation of the operculorubral or rubro-bulbar pathways.

The afferent and efferent fibers of the red nucleus play apparently a very important rôle in the causation of a number of motor disorders.

Choreo-athetotic manifestations, posthemiplegic tremors, are met with in a variety of lesions in which some portion of the afferent pathway of the red nucleus is involved. The motor phenomena in such cases are probably due either to a direct irritation of the red nucleus or else to an interruption of the cortical fibers whose mission normally is to regulate the automatic function of the nucleus. According to the part of the afferent pathway involved and according to the tissue in the close vicinity implicated, the motor phenomena will assume a different picture (Archambault).

#### CORPORA QUADRIGEMINA

In the sections of Occipital Lobe and Temporosphencoidal Lobe, it was mentioned that the anterior quadrigeminal bodies are connected with the former through the optic radiations and are, therefore, concerned in the function of vision, that the posterior quadrigeminal bodies are connected with the cortex of the latter and consequently concerned in the function of hearing.

Diseases confined exclusively to the quadrigeminal bodies are rare because of the simultaneous involvement of the adjacent portions. However, in a few cases of tumors limited to the quadrigeminal bodies the following symptoms were observed:

*Anterior Bodies.*—Ptosis, paralysis of bilateral associated movements of the eyes, upward and downward, also limitation of lateral movements of the eyes, finally paralysis of convergence. Ophthalmoplegia is therefore characteristic. It is due to an involvement of the oculomotor nuclei situated beneath the quadrigeminal bodies. The pupils are usually unequal and dilated. In the beginning the vision is not impaired, but later in the course of the disease, when secondary changes set in the optic nerves, the vision becomes defective.

*Posterior Bodies.*—When the posterior quadrigeminal bodies are affected, the hearing becomes deficient. Some observations point to the fact that a lesion of one posterior quadrigeminal body causes impairment of audition on the opposite side.

*Motor Symptoms.*—According to Nothnagel, there are a cerebellar gait and loss of equilibrium in standing. Paralysis is present only in advanced stages of the disease when the tumor commences to press on the motor tracts. According to Nothnagel, when the cerebellar gait makes its appearance as the first symptom, and especially in association with the ocular phenomena (*see above*), the diagnosis is certain. The reflexes become altered only when the tumor involves the motor pathway; then the patellar tendon reflexes are exaggerated and the toe phenomenon is present. As in cerebellar diseases, the knee-jerks may be either diminished or abolished. In some recorded cases there was present a tremor of the head, arms and legs.

Recent experiments performed on dogs by D. L. Monaco,<sup>70</sup> of Rome, gave the following results: A lesion of the anterior quadrigeminal body influences the general sensibility (contralateral hypesthesia), produces a modification of facial mimicry, an exaggerated patellar tendon reflex on

the opposite side, weakened vision in the entire visual field and trophic changes of the conjunctiva and cornea, but there are no changes in the motility of the ocular globe. A lesion of the posterior quadrigeminal body weakens the auditory function.

A lesion of the quadrigeminal bodies has no influence on the general nutrition nor on the skin and hair. It produces no change in the cardiac and respiratory rhythm. Its influence on phonation is evident, as the animal does not cry even if it is hurt.

## IX. INTERNAL CAPSULE

Together with the basal ganglia (thalamus opticus and corpora striata), between which it is situated, the internal capsule forms the most frequent seat of hemorrhage, embolism and thrombosis. The reason of it lies in the fact that the small vertical arteries which are distributed to those parts, namely, the lenticulostriate and lenticulothalamic arteries, having no collateral branches, are under a relatively high pressure and therefore are more apt to rupture than cortical vessels, which branch a great deal. Durand-Fardel has shown that these same arteries develop frequently miliary aneurysms which means degeneration of vessel wall and hence rupture. They were deservedly called by Charcot "arteries of cerebral hemorrhage." When the vessel wall is altered, miliary aneurysms are apt to form (Charcot and Bouchard). The important exciting element is the rise of arterial pressure which, when it reaches the short terminal arteries of the internal capsule (and of the central ganglia), facilitates their rupture. In aged individuals Ferland called attention to a special state of cerebral tissue characterized by small cavities (lacunes), in the center of which is seen a small artery. As the blood-pressure is invariably increased in advanced age, the atheromatous central artery is easily ruptured when the blood-vessel is under high tension.

The most important consequence of cerebral hemorrhage or softening is its remote effect on the nervous tissue beneath and in the immediate vicinity of the area destroyed either by the blood clot or by the softening. Secondary degenerations, which rapidly set in, are the usual result. They may be traced through an entire tract.

A lesion, for example, in the posterior limb of the internal capsule will be followed by a descending degeneration in the entire motor pathway, even in the lowest portion of the spinal cord. The degeneration is characterized at first by disappearance of the myelin and nerve-fibers which are ultimately replaced by connective tissue, and a scar is thus formed.

The posterior limb of the internal capsule consists of two portions: the anterior two-thirds are exclusively motor and the posterior third exclusively sensory in function ("carrefour sensitif" of Charcot). In 1859, Türk showed that lesions in the posterior segment of the capsule were followed by hemiplegia accompanied by a diminution of general

and special sensation on the opposite side of the body. Charcot subsequently studied closely the subject of sensory disturbances caused by an involvement of the internal capsule and formulated his ideas by naming the posterior portion of the posterior limb of the capsule "carrefour sensitif." The hemianesthesia concerns not only the general sensations (touch, pain, temperature, muscular sense, etc.), but also the special sensation, viz., vision, audition, taste and smell. For a long time this conception of the function of the posterior capsular segment remained classical and was adopted by many writers. When, later, the character of capsular hemianesthesia was studied more closely, it was observed that those complete losses in the domain of special and general sensations were exactly like those observed in hysteria or else some of those so-called typical cases presented an association of organic and functional hemianesthesia. It was Dejerine and Long, in 1899, who commenced to throw doubt on Charcot's conception. With exact anatomical data on hand, they demonstrated that, if the lesion destroys the retrolenticular portion of the internal capsule in the lower thalamic area and cuts at the same time the visual bundle of fibers, there will be a lateral hemianopsia. If on the other hand the lesion lies higher and thus does not involve the visual bundle, there will be no disturbance of vision.

In the domain of hearing exact restrictions must also be made. The auditory neurons coming from the first temporal convolution pass through the posterior limb of the sublenticular portion of the internal capsule on their way to the internal geniculate body and posterior quadrigeminal tubercle. When these fibers are destroyed by a lesion in the sublenticular segment of the capsule, the auditory disorder is not persistent.

The same remarks are applicable to the senses of smell and taste. The olfactory fibers coming from the cornu ammonis pass through the posterior root of the olfactory trigone to the mammillary tubercle, but do not pass through the internal capsule. The taste fibers are located probably in the same pathway.

It is, therefore, evident that the involvement of the special senses in capsular hemianesthesia is not only not constant but it does not possess the same characteristics which formerly were considered typical. As to the general sensations, while their involvement in capsular hemianesthesia is not contested, nevertheless their localization is debatable. Careful anatomical examinations revealed in almost all cases a simultaneous involvement of the internal capsule and the thalamus opticus. Moreover, Dejerine and Long have found in some cases integrity of the posterior capsular segment, in other cases integrity of the thalamus, but instead an involvement of the tracts connecting the latter with the cortex. Furthermore, they have shown that a hemianesthesia will be present only when the lesion affects the posterior and inferior nucleus of the thalamus where the fibers from the island of Reil terminate. Finally the same authors brought forth anatomical proofs of the fact that a lesion of the posterior portion of the posterior limb of the internal

capsule with complete integrity of the thalamus may produce a hemiplegia without the least disturbance of sensations.

To sum up, in view of intermingling of the thalamocortical and corticothalamic fibers with those of the internal capsule, a capsular hemianesthesia is possible only when the lesion implicates the fibers going to and coming from the thalamus or the thalamus itself. A persistent hemianesthesia presupposes a direct involvement of the thalamus. The old conception of "carrefour sensitif," as understood originally, can no longer be maintained in view of the carefully observed anatomical facts. For *differential diagnosis* between a capsular (central) and cortical hemianesthesia, see section on Parietal Lobe.

## X. CORPUS CALLOSUM

**Anatomical Considerations.**—A horizontal cut of a whole brain enables one to follow the corpus callosum through the hemispheres to the external border of the lateral ventricles. A sagittal cut of the corpus callosum will reveal anteriorly the knee which, when it reaches the base, is reduced to a thin layer of white matter, the white commissure of Henle. The posterior end of the corpus callosum, the splenium, is located over the quadrigeminal bodies and the pineal body. Sherrington,<sup>80</sup> in his experimental work on the cortex, observed degenerated fibers in the corpus callosum on the opposite side. The same condition was seen by Muratow<sup>81</sup> in experimental lesions of the motor area. Dejerine<sup>82</sup> and others report similar findings in pathological states of the cortex.

Extensive anatomical studies have shown that the fibers of the corpus callosum are connected with every portion of the cortex except the olfactory lobe and the tip of the temporal lobe. Dejerine thus summarizes the topographical arrangement: (1) The trunk of the callosum has superior, inferior and median fibers. The superior fibers are connected with the frontal, parietal, temporal, first limbic, paracentral lobes and precuneus; the inferior fibers with the operculum and posterior portion of the temporal lobe; the median fibers with the frontal, middle portion of the rolandic area and second parietal convolution. (2) The knee of the callosum is connected with the external and orbital surfaces of the frontal lobe. (3) The splenium is connected with the posterior portion of the occipital lobe, with the lingual lobe, fusiform lobule and the cuneus.

The question of whether the fibers of the corpus callosum are connected with the cortex of the opposite hemisphere has not been entirely settled. In the present state of our knowledge one may say that certain cases show that some fibers originate in the same hemisphere and others in the opposite hemisphere. As to the relation of the fibers of the corpus callosum to the internal capsule, the latest experimental work demonstrates that the former does not send any fibers into the latter. The external capsule is equally free from fibers of the corpus callosum.



**Function of the Corpus Callosum.**—Experimental studies have been exceedingly unsatisfactory and for the following reasons: (1) Great difficulties have been encountered to limit sections or other manipulations to the callosum in addition to the hemorrhages. (2) Electrical stimulation of the callosum always gave phenomena of diffusion of the electrical current to the neighboring tissue. The physiology of the corpus callosum was best studied from pathological conditions, strictly confined to this body, especially in cases of tumors. There are now about one hundred such cases in the literature.

**Callosal Syndrome.**—A careful analysis of these cases brings out the following semeiology of *callosal syndrome*. There are two varieties of disturbances: (a) psychic and (b) psychomotor.

**PSYCHIC SYMPTOMS.**—Raymond gives the following pictures: A break in association of ideas; bizarre mannerism and action; disturbed memory, especially for recent events and for topographical definitions; modification of character: irritability, variation of humor, carelessness.

**PSYCHOMOTOR SYMPTOMS.**—*Motor apraxia*, as described originally by Liepmann, is the most conspicuous manifestation. Although it is not present in absolutely every case, nevertheless it is sufficiently frequent to be considered as characteristic of a callosal lesion. It is a very serious manifestation. It will be discussed in a special section.

*Hemiplegia* is very frequent and what is particularly characteristic is its progressive development. The face is usually spared. Flaccidity of the limbs is most frequent, contractures are observed in the minority of cases. Bilaterality of paralysis is less frequent than unilaterality. Monoplegia or hemiplegia on one side and monoplegia on the other side may all be observed. Tremor, choreiform movements, are seen sometimes. Ataxia, disturbance of equilibrium and of gait have been observed in some cases. The tendon reflexes are exaggerated in the majority of cases. Disturbances of speech are frequent. They may simulate the speech of paretics; dysarthria, aphasia, staccato speech, have all been observed. A muttering speech is sometimes present; the patient moves his lips but does not make sounds. Cranial nerves are usually not involved.

**SYMPTOMS ACCORDING TO SEAT OF LESION.**—Duret,<sup>82</sup> in his work entitled "*Tumeurs de l'Encéphale*," gives the following interesting classification of symptoms according to the seat of the lesion in the corpus callosum:

(1) *Anterior Portion of Callosum.*—Intellectual feebleness; dysarthria; disturbance in the motility of the face, tongue, lips, trunk, more rarely of the upper extremities. All these manifestations are bilateral but of various intensity according to the side involved.

(2) *Middle Portion of the Callosum.*—Stupor; titubation; astasia-abasia; paresis of all four extremities but of unequal intensity.

(3) *Posterior Portion of the Callosum.*—Paresis of the lower extremities; ataxia of cerebellar type; hemianopsia.

**Apraxia.**—The symptom *apraxia* stands out most prominently in the majority of cases of callosal lesions. By this name is understood a disorder in the faculty of using the limbs for purposive movements in spite of absence of paralysis or of ataxia. It was Liepmann<sup>54</sup> who first observed such a case and had the opportunity of verifying his clinical conclusions by post-mortem findings. His patient, a man of forty-eight, of good intelligence, presented a peculiar motor disturbance on the right side. He recognized objects, knew their use, but he could not handle them properly with the right hand, while the handling with the left hand was correct. Besides, certain simple gestures of everyday occurrence were carried out by him in the most irregular and inadequate manner. Liepmann studied the subject from every standpoint, built up his hypothesis of apraxia and discussed all its clinical variations and anatomical localizations. Since then, a number of observations have appeared in the literature.

To carry out a given voluntary act various psychological and physiological phenomena must necessarily follow each other in a certain order, viz.: (1) Stimulation of the sensorium, which at once conceives synthetically the act as if it were accomplished; gradually it figures out the elementary acts necessary for a final realization of the entire act. (2) The mental representations elaborated by the sensorium are transmitted to the psychomotor or ideational-motor center in which the motor images are aroused; otherwise speaking, in this phase the passage of the original idea to the motor idea takes place. (3) The motor idea discharges motor stimulations necessary for execution of the desired act.

It is, therefore, evident that according to the element involved, there may be a great variety of pathological combinations. Ordinarily we meet with three main forms of apraxia, viz.: ideational, ideational-motor and motor. Apraxia is *ideational* when the first phase is affected. For example: to drink out of a tumbler the patient does not know that he must take it in his hand, carry it to his mouth and incline the tumbler gradually, although he knows the name of the object and the purpose of the desired act.

Apraxia is *ideational-motor* when the motor images for a voluntary act are not aroused although the conception of the act is not disturbed. In the above example, the patient does not know how to take hold of the tumbler and carry it to the mouth.

Apraxia is *motor* when the patient knows what to do with the tumbler, that he has to contract the muscles of the hand, but in his attempts to do so, he does not succeed in properly using the muscles. The act of execution does not correspond to the conception; correct movements are replaced by purposeless ones; the muscular contractions are performed without any adaptation to the object desired, without order, and without coördination.

A. IDEATIONAL APRAXIA.—As we are here in presence of a deep intellectual disorder, this form of apraxia may be met in a variety of cerebral conditions.

In psychoses, in which memory, attention and association of ideas are disturbed, in dementias which are global and diffuse, apraxia will necessarily be present. Ideational apraxia is frequently associated with aphasia. The relation of one to the other is interesting. In right-handed persons the aphasia is due to a lesion in the left hemisphere. Apraxia also is very frequently due to a left-sided lesion in right-handed individuals. Broca's area controls bilateral muscles, so does the corpus callosum; the latter is the most probable seat of eupraxia, which regulates the movements of both sides of the body. A motor aphasic can move the muscles of the lips, throat and tongue, but cannot coördinate them for proper speaking. An apraxic can move his limbs, as there is no paralysis, but he cannot coördinate the movements of the limbs in order to execute a volitional act. Some aphasics cannot speak spontaneously because they are unable to recall auditory word images; apraxics cannot move their limbs spontaneously because they cannot recall kinesthetic images.

Ideational apraxia, because of a disturbed intellectual substratum, may be encountered in diffuse cerebral lesions, in tumors of the brain, in uremic intoxication, in confusional states of any origin. It has no special localization.

B. IDEATIONAL-MOTOR APRAXIA.—In this form of apraxia the patient knows perfectly what act to execute, but the execution itself is imperfect. When, for example, he is told to take a match out of a box, his general conception of the act is good; nevertheless he will let the box drop and spill the matches. While an ideational apraxic gives the impression of a mentally affected individual, the ideational-motor apraxic gives the impression of an awkward personality. In case of complex acts, two peculiarities are observed: When the act is gross, such as to fill a glass or to open a letter, each component simple movement is done with difficulty, viz., without precision, and the movement is either overdone or underdone, as we observe in cerebellar or cerebral ataxia. When the act is fine or delicate, such as in sewing, for example, its execution is impossible. Dejerine lays special stress on these phenomena, as they enable one to differentiate them from true ataxia: in ataxia the incoördination is equally observable for both fine and gross acts; in apraxia the ataxiform movements are evident only for gross acts. Another important characteristic of the ideational-motor apraxia is the integrity of the psychic functions, while in ideational apraxia the involvement of the mentality is most conspicuous. Moreover, in the former an effort of the attentive power does not modify the apraxia in simple and complex acts, while the contrary is observed in ideational apraxia. Finally, in the ideational apraxia, there is a diffuse and generalized condition because of the character of its pathological substratum (*see above*). On the contrary, in the ideational-motor form the apraxia may concern only one side of the body, one arm, one leg or only a few muscles. All depends upon the fibers connected with the special cortical centers of the limbs.

The *pathological anatomy* of the ideational-motor apraxia presents very important features. The predominant view is that the lesion is localized in the left parietal lobe and especially in the supramarginal gyrus. The cases of Kroll,<sup>85</sup> Strohmayer,<sup>86</sup> von Stauffenberg,<sup>87</sup> Fearn-sides,<sup>88</sup> also the statistics of Liepmann and Kleist, finally the most recent cases of Ch. Foix, are all in favor of this special localization. The apraxia resulting from such a lesion will be present in the right arm. By analogy one is apt to place apraxia of the left arm in the right hemisphere. Such a lesion has so far not been observed, and besides, cases have been reported of left arm apraxia without any discoverable lesion in the right hemisphere. To explain such occurrences one must bear in mind the cases of Liepmann and Maas,<sup>89</sup> of Goldstein,<sup>90</sup> and of Wilson.<sup>91</sup> In all the cases the involvement of the corpus callosum plays a most important rôle. There are also cases of left apraxia accompanied by hemianesthesia, astereognosis and other sensory disturbances on the same side, in which lesions were found in the right hemisphere, so that the apraxia may have been caused by those right-sided lesions without incriminating the corpus callosum. However, the rôle of the right hemisphere in left-sided apraxia is not yet entirely determined and remains problematical. All the cases reported lead to the conclusion that a lesion of the left hemisphere, when it is isolated, may cause a bilateral apraxia with predominance on the right side. When apraxia predominates on the left, then there is an important lesion in the corpus callosum and perhaps an associated lesion in the right hemisphere.

From the foregoing remarks it is evident that the rôle of the left hemisphere is fundamentally preponderant in conceiving and in carrying out voluntary movements. It accumulates certain impressions acquired by the right hemisphere. On the other hand, it controls the acts executed by the right hemisphere; the latter acts, but the left hemisphere makes it act. Its rôle is exclusive in right-sided apraxia and partial in left-sided apraxia. In the latter case the transmission of the kinetic images is accomplished through the corpus callosum through which travels a sort of a double current, viz., one from the right to left, the other from the left to right.

C. MOTOR APRAXIA.—It is the result of a break between the chief idea of an act and its carrying into execution. The center of the limb, with its kinetic memories, is intact, but, in view of a break in its associations with other centers, the transmission of the details of which each act is composed to the center of the limb is interrupted. Otherwise speaking, idea and kinetics part company. This parting may present itself in two ways: (1) Sometimes simple movements may be executed correctly, but not at the proper time, not when the patient has decided to carry them out; this is, of course, due to lack of harmonious action of the center of the limb and the brain in general. (2) Sometimes the execution of the act is out of proportion, clumsy, awkward or too gross. It is limb-kinesthetic apraxia of Liepmann. It corresponds

to Meynert's "motor asymbolia" or Nothnagel's "Seelenlähmung." Anatomically, motor apraxia is presumably due to a fine and superficial alteration in the motor center of the opposite arm, insufficient, however, to produce a real paralysis.

Motor apraxia may sometimes be associated with another phenomenon to which Neisser<sup>92</sup> gave the name of "perseveration." In this condition the patient repeats a certain act when asked to execute another act or when he himself wishes to execute another act. Pick called it "pseudo-apraxia." The same phenomenon may be observed in a different form: the patient continues performing a certain act although he is told to discontinue it. Liepmann's patient continued writing letters (*loc. cit.*), Campbell's<sup>93</sup> patient continued shaking hands, Breukink's<sup>94</sup> patient kept on peeling potatoes indefinitely. According to Liepmann, the idea of the abnormal persistence of a certain movement is due to an interference with the carrying out of other innervations along other pathways.

**GENERAL CONSIDERATIONS OF APRAXIA.**—Apraxia is frequently overlooked, as it is a discrete phenomenon. It is only through a systematic examination that it can be revealed. In examining for motility one must test the patient for simple and complicated movements, automatic and reflective movements. Handling objects spontaneously and on order, writing, copying, etc., are all necessary efforts. Such an analysis will enable one to determine a true apraxia and conditions which may simulate it in paralysis, ataxia, choreo-athetotic movements, tremors, aphasia. By a careful analysis a distinction will be made between the various forms of apraxia, viz., motor, ideational and ideational-motor.

Laignel-Lavastine and Boudon advise the following system of movements in testing for apraxia: (1) Walking, sitting down or getting up (autokinetic movements). (2) Simple movements: close the eyes, open the mouth, put out the tongue, raise an arm. (3) Show the right or left eye or ear, comb the hair. (4) Salute in a military fashion, make the movement of a kiss. (5) Make the movement of catching a fly. (6) Fill a glass with water, seal an envelope.<sup>95</sup>

## XI. CEREBRAL VENTRICLES

### A. THIRD VENTRICLE

The diseases of the third ventricle have reference chiefly to tumors. There are in the literature about thirty-two cases, all with tumors. A tumor situated within the ventricle will not only produce pressure on the neighboring tissue, but will also invade the opening into the lateral ventricles through the foramina of Monro, into the fourth ventricle through the aqueduct of Sylvius and into the subarachnoid space through the foramen of Magendie. The tissues lying on either side of the third ventricle are the optic thalami, and, below, the chiasma

and the hypophysis. Within the ventricle are placed the choroid plexuses, which are the chief source of the cerebrospinal fluid; if these are irritated, oversecretion will take place, hence internal hydrocephalus. If the foramina connecting the third with the lateral ventricles or with the aqueduct of Sylvius are obstructed, there will be predominance of accumulation of fluid in the lateral or fourth ventricles. Thus it is evident that the morbid manifestations during life will present great varieties according to the parts involved.

An analysis of all the cases recorded leads to these conclusions: Apart from general symptoms of brain tumors, viz., headache, vomiting, choked disk, the following must be considered. When the foramina of Monro are obstructed, the lateral ventricles become dilated; symptoms of hydrocephalus are present (*see below*). Paresis of one or both limbs and symptoms of the thalamic syndrome will be present (*see Optic Thalamus*). When the aqueduct of Sylvius is invaded and its walls are being pressed upon, there will be present: paralysis of associated ocular movements and of convergence upwards; ataxia of station, gait and voluntary movements; ptosis (sometimes), dilated pupils and disturbed light reflex; a paretic condition of the limbs, change of tendon reflexes. Mental symptoms, such as apathy, somnolence, are probably due to transmitted pressure on the cortex. (For the literature on diseases of the third ventricle, the reader is referred to P. Stewart,<sup>96</sup> Howell,<sup>97</sup> J. Turner,<sup>98</sup> Weisenburg,<sup>99</sup> Pollock,<sup>100</sup> and Bassoe.<sup>101</sup>)

If a tumor is situated in the lower portion of the third ventricle, it will produce pressure upon the hypophysis and especially upon the infundibulum. In a recent observation by Claude and Lhermitte,<sup>102</sup> a cystic mass was strictly limited to the inferior portion of the third ventricle and infundibulum, and gave place to a group of symptoms which were quite characteristic and to which the authors gave the name of "infundibular syndrome." The following were the manifestations: Bitemporal hemianopsia; dysarthria (which was probably due to involvement of the neighboring inner bundles of crura and especially of the geniculate fibers); psychic disturbances; attacks of narcolepsy; circulatory disturbances (crises of tachycardia, arrhythmia); persistent thirst; polydipsia and polyuria. As to the nature of these symptoms, they were probably of sympathetic origin. This view is in keeping with the modern theory of the anatomists who believe in the existence at the base, between the bulb and the infundibulum, of centers influencing the sympathetic system.

### *Hydrocephalus*

**Physiology.**—Hydrocephalus is characterized by an increased accumulation of cerebrospinal fluid in the ventricles. The old classical division into acute and chronic, internal and external, congenital and acquired, will have to be modified in view of the newly acquired information, concerning the mechanism of formation and absorption of the cerebrospinal fluid. Magendie,<sup>103</sup> as far back as 1842, demonstrated experimentally that free communication exists between the ventricles and the

subarachnoid space by means of a foramen which now bears his name, that the cerebral and spinal subarachnoid cavities are freely communicating with each other, that the aqueduct of Sylvius or the foramen of Magendie may be obstructed in hydrocephalus. He thought that the source of origin of the cerebrospinal fluid was the pia alone.

The recent experimental work of Dandy and Blackfan, of Frazier and Peet, Dixon and Halliburton, Thomas, Weed and Cushing and others puts a different light on the physiology of the cerebrospinal fluid.

It has been shown that the cerebrospinal fluid forms in the ventricles, that it escapes through the aqueduct of Sylvius, that, if the latter is obstructed, internal hydrocephalus results. That this obstruction is a very important element is seen from the fact that the hydrocephalus will form even if the choroid plexuses of the lateral ventricles have been almost completely extirpated. Experiments have also shown that a low ligation of the Galen vein (but not a high) leads to an internal hydrocephalus.

Schmorl<sup>104</sup> expressed the opinion that the choroid plexuses are not the only source of the cerebrospinal fluid and that the latter may be formed in the subarachnoid space. Indeed, in cases of internal hydrocephalus, in which the foramina of Luschka and Magendie were found obstructed, there was also a large amount of fluid in the subarachnoid space, presumably through the process of transudation. Experimental, physiological and anatomical investigations concerning the formation of cerebrospinal fluid, based on its chemical composition, its structure and the degree of its permeability, on the influence of drugs on its production, all lead to the conclusion that the choroid plexuses (also probably the ventricular ependyma) are the chief sources for the secretion of cerebrospinal fluid, that the latter is rapidly formed by means of venous stasis, if the collateral circulation is insufficient, that, in view of the similarity of the saline content of the blood and of the cerebrospinal fluid, transudation may be also considered as one of the causative factors of the fluid.

Magendie (*loc. cit.*) demonstrated that after draining the subarachnoid space to the utmost, an equal amount of cerebrospinal fluid could be obtained a few hours later; also that coloring matter injected into the subarachnoid space could be recovered in the urine and jugular veins. Hence, he proved that the cerebrospinal fluid possessed an active circulation, that it could be absorbed and it could be reformed. Recent experimental observations have shown that the cerebrospinal fluid can be absorbed and renewed about every four hours, that the absorption takes place into the blood and particularly into the capillaries of the subarachnoid space, that the latter is the chief area of absorption, that the ventricles take very small if no part in the process of absorption, and finally that the old view of Key and Retzius concerning the rôle of the paccionian bodies in the process of absorption can no more be maintained.

**Forms of Hydrocephalus, Their Etiology and Relation to Other Diseases.**—Since the cerebrospinal fluid forms in the ventricles and is

absorbed from the subarachnoid space, it stands to reason that the normal or disturbed equilibrium of the fluid will depend upon the relation of its production to the process of absorption, also upon the conditions of communication between both spaces. It is, therefore, evident that internal hydrocephalus may develop when absorption is defective or delayed, and it may develop when there is an obstacle to the drainage from the ventricles into the subarachnoid space.

Accordingly, internal hydrocephalus may be divided into two main forms: (1) *communicating* and (2) *obstructive*.

(1) In the *communicating* form the defective absorption of the cerebrospinal fluid was demonstrated by the phenolsulphonephthalein test. By introducing this drug into the ventricles and by examining later the spinal fluid for the drug, it was possible to reveal its presence within one to seven minutes, thus showing the integrity of the communication between ventricles and subarachnoid space. As to the absorption, it is decidedly deficient and this is due either to the presence of adhesions in the subarachnoid space, or to some changes in the meninges themselves. (2) In the *obstructive* form of internal hydrocephalus there is an obstacle in any of the foramina between the ventricles, which mechanically interferes with the drainage of the cerebrospinal fluid. If the foramen of Monro is occluded, the lateral ventricle on the corresponding side will be enlarged. If the aqueduct of Sylvius is occluded, the third and lateral ventricles will be dilated. If the foramina of Luschka and Magendie are blocked, all the ventricles will be dilated.

Besides these two chief causes, viz., faulty absorption and mechanical obstruction, there may be other factors in the production of internal hydrocephalus. Venous stasis due to obstruction of veins of Galen by a cerebral (especially at the base) and cerebellar tumor may be one of these factors. The above mentioned experiment by ligation of the large vein of Galen (Dandy and Blackfan) is proof of this contention. It belongs to the so-called "*symptomatic hydrocephalus*." In the same group may be placed cases of acute or chronic serous meningitis which may produce an excessive exudation of fluid in the ventricles (Quincke). The *acute* form is met with in gastro-intestinal disorders; the effusion is more frequently in the ventricles than in the subdural space. Hydrocephalus may also be symptomatic of phlebitis of the sinuses.

The *chronic congenital* variety of hydrocephalus is always associated with malformations of the brain. The hemispheres of the cerebrum and cerebellum may be entirely wanting (anencephaly), may present absence of certain lobes or of other portions (as corpus callosum, etc.) or they may be reduced in size (microcephaly or microgyria). With the congenital hydrocephalus are frequently associated symptoms of arrested development of various tissues or organs of the body (spina bifida, ectopia of organs, flatfoot, harelip, etc.).

Hydrocephalus seems to stand pathogenetically close to *hydromyelia* and *syringomyelia*. Schlesinger observed in 56 cases of syringomyelia 4 cases of hydrocephalus. Homén found 5 cases of internal hydrocephalus in 12 cases of syringomyelia, Hinsdale 15 cases in 150 cases



of syringomyelia. This fact, together with the occurrence of syringo- or hydromyelia in spina bifida, anencephalia, porencephaly, cerebral gliomata, microgyria, observed especially by Schüller<sup>108</sup> and also by Dejerine, Oppenheim and others, all tend to show that there must be an etiological relation of a teratological nature, viz., developmental anomaly



FIG. 7.—HYDROCEPHALUS, SHOWING EXTENSIVE DILATATION OF CEREBRAL CAVITIES  
(Gordon, Courtesy *Journal of Nervous and Mental Diseases*.)

of both portions of the cerebrospinal axis. A striking example of a hydromyelic form of cerebral cavities, also of the central canal in the spinal cord, was described by the author<sup>108</sup> in 1916. There was an enormous dilatation of the central canal of the cord and of all the ventricles of the brain with extraordinary deformity of the surrounding nervous tissue.

In *sypphilis*, *tuberculosis*, *alcoholism*, *rickets* and *trauma*, hydrocephalus has been observed, but these factors can be admitted as causes only if they produce localized lesions in the cerebrospinal spaces, thus interfering with drainage either by mechanically obstructing the foramina or by interfering with the absorption of the cerebrospinal fluid.

The recognition of the above-mentioned two types of internal hydrocephalus is of the highest therapeutic importance. As clinically there are no special manifestations differentiating one from another, the only reliance is the phenolsulphonophthalein test. If 1 c.c. of a neutral solution of phenolsulphonophthalein is injected into the lateral ventricle, 30 to 60 per cent. of the drug should, under normal conditions, be recovered from the urine in two hours; also the spinal fluid should be stained in from 3 to 8 minutes.

Frazier and Peet<sup>107</sup> have also shown that if, after withdrawing 1 c.c. of spinal fluid by lumbar puncture, 1 c.c. of neutral phenolsulphonophthalein solution is injected into the spinal cord, a trace of dye should appear in the urine in 10 minutes and the entire amount excreted in two hours. Consequently, in cases of the obstructive type of internal hydrocephalus the absorption of the drug from the subarachnoid space and the excretion of the kidney are practically normal. In cases of the non-obstructive or communicating type, in which absorption is deficient, the appearance of the dye in the urine is delayed and the amount of dye excreted is correspondingly low.

**Symptomatology.**—The most conspicuous initial symptom in *young children* is the gradual increase of the size of the head. In some cases, however, spasticity of the extremities or convulsions may precede the abnormal development of the head. The head is usually enlarged in its transverse diameter, the sutures are separated, the forehead is high and protruding. The last is divided to the root of the nose by the enlarged fontanel. The root of the nose is broad. The lateral fontanel being much opened, the temples are also protruding. The hair on the head is sparse. The facies is striking: it is pale and thin, the subcutaneous veins are prominent and swell especially during crying spells. The eyes converge, are protruding and directed downwards. The pupils are partly covered by the lower eyelids. Vision is very frequently and quite early affected, because of pressure exerted by the dilated third ventricle upon the chiasma. Optic neuritis, followed by optic atrophy, is a common occurrence. Strabismus is usually present. Horizontal nystagmus is frequent. The other cranial nerves do not present, as a rule, any involvement. The patient is unable to hold the head erect, as the latter has a tendency to fall backwards or sidewise, as if it were a lifeless part of the body. Rotating, however, is possible when the patient lies on his back. The extremities and trunk show marked impairment of nutrition. Nervous symptoms are mainly motor. Convulsions appear early; they are due to pressure upon the cortex produced by the dilated ventricles. Rigidity of the extremities is present, and especially of the adductor muscles; the tendency to cross the legs is particularly pronounced. In advanced stage of the disease, the arms and the trunk be-

come also spastic. The increase of the patellar tendon reflex is an early symptom. The toe phenomenon is present. The gait is difficult and uncertain.

The general sensibility is rarely affected.

The vegetative system is usually not disturbed, with the exception of vomiting and constipation, which are ordinarily present.

The psychic functions are usually involved. Mental development is frequently arrested. Idiocy or only feeble-mindedness may be present.



FIG. 8.—HYDROCEPHALUS, SHOWING CHARACTERISTIC CONTOUR OF THE HEAD.

In mild cases the psychic functions remain intact. Speech and the ability of walking develop late. As the disease is usually progressive, the intracranial tension and pressure continue to increase. Headache is, therefore, a frequent symptom and the sounds of suffering made by the patient are characteristic. They are known as the "hydrocephalic cry," a sort of a shallow scream.

The *symptoms in adults* are somewhat different in their development than those in very young children. As the fontanels do not separate, the enlargement of the head is not so conspicuous as in children. The condition may then be confounded with cerebral tumor. Indeed, the general symptoms of the latter are all present, viz., headache, vertigo, optic

neuritis, convulsions, stuporous state. The diagnosis is difficult. However, early loss of upward movements of the eyes, early impairment of light reflex, early optic atrophy, which is not infrequently ushered in with bitemporal hemianopsia and rapid blindness, progressive bilateral rigidity with increased knee-jerks, ankle-clonus and toe phenomenon—are all almost pathognomonic of hydrocephalus in adults. The reason of the ocular phenomena is to be found in the downward pressure exerted by the distended third ventricle on the nucleus of the third nerve.

**Pathology.**—In the beginning of this chapter the mechanism of formation of hydrocephalus was extensively discussed.

Among all the ventricles the lateral ones are chiefly affected. The amount of fluid is variable; two quarts is not a very rare occurrence. The fluid is, as a rule, clear, with a specific gravity of 1.005 to 1.010. Its reaction is alkaline. It contains a small quantity of albumin (0.25 to 1 per 1000) and a noticeable amount of chlorids (more than in the plasma of the blood); also some carbonic and phosphoric acids and a reducing substance, probably grapesugar. The pressure under which the fluid appears on lumbar puncture may be very high, provided the communication between the ventricles is intact.

The distention of the lateral ventricles may be symmetrical on both sides or may be more pronounced on one side than on the other. The lining membrane of the ventricles and the choroid plexuses are thickened. According to Anton, the corpus callosum and fornix are the first to undergo atrophy. The effect of pressure is carried to all parts of the cerebrum, basal ganglia and cortex. The convolutions are flattened and the fissures disappear. In extreme cases the entire cerebrum presents two large cysts, the walls of which are thin (*see* author's case of hydro-encephalia reported above). In hydrocephalus occurring very early in life myelinization of the nerve fibers is arrested. The pyramidal fibers through their entire course are either not developed or arrested in their development. In hydrocephalus appearing later in life, the pyramidal tract is in a state of secondary degeneration. The cranial bones become atrophied, the diploë disappears. The not infrequent association of various malformations in the congenital cases of hydrocephalus was discussed above.

**Diagnosis.**—As the large size of the head is the most prominent symptom of hydrocephalus, the latter may be confounded with rachitis, in which the head may be also voluminous. In the latter affection, the cranium is not uniformly enlarged, the fontanels are not bulging, the nervous and intellectual manifestations of hydrocephalus are absent. Finally, the usual stigmata of rickets (deformities of limbs, etc.) will render the diagnosis comparatively easy.

**DIFFERENTIAL DIAGNOSIS.**—*Acute cerebral affections* of early infancy may simulate hydrocephalus. It is important in all such cases to examine frequently the state of the fontanels and of the sutures. *Tuberculous meningitis* in infants may also resemble hydrocephalus. It should be remembered that tuberculous meningitis occurs habitually in children that are weak or directly tuberculous. Moreover, the cerebrospinal

fluid in tuberculous meningitis presents special features, viz., increase of albumin, and especially lymphocytosis, and the presence of tubercle bacilli.

The greatest difficulty is found in differentiating internal from external hydrocephalus. However, the enlargement of the head in ventricular forms is more rapid than in the external variety. Besides, at the beginning of external hydrocephalus the symptoms are those of hemorrhagic meningitis or pachymeningitis, and the latter affections lead rapidly to death. A lumbar puncture in hydrocephalus will bring out a clear fluid, while in hemorrhagic pachymeningitis it will bring a yellowish or hemorrhagic fluid rich in albumin. Retinal hemorrhages are found in the latter, but not in the former.

**Treatment.**—In view of the fact that syphilis may sometimes be an etiological factor, it is advisable to submit every case of hydrocephalus to a thorough course of **antiluetic remedies**. As gastro-intestinal disorders may sometimes be a cause of hydrocephalus, appropriate diet with **intestinal antisepsis** should be tried.

Frazier (*loc. cit.*) claims having obtained very favorable results from **thyroid extract**, basing its use on its rôle of a depressor on the choroid plexus through which the secreting of cerebrospinal fluid is reduced.

The predominating treatment at present is **surgical**. Although complete restoration of lost cerebral function cannot be expected from the best procedures, nevertheless it has been observed that symptoms of pressure may retrogress and lost vision may be partly restored.

**Lumbar puncture**, if cautiously performed, may be harmless: sudden withdrawal of large quantities of fluid must be avoided, as sudden decompression of the brain may be fatal. As the fluid reforms rapidly, frequently repeated punctures will be necessary.

When operative procedures on the brain are decided upon, before doing an operation, a test with phenolsulphonephthalein should be performed (*see above*) in order to determine whether a given case of hydrocephalus is of the obstructive or communicating type. In the obstructive variety, **puncture of the corpus callosum** (*Balkenstich* of Anton and Bramann) and **probing the lateral ventricles** are the most effective method. Great amelioration has been obtained from this procedure in the field of general symptoms, viz., headache, vertigo, vomiting and ocular disturbances. This operation provides an outlet for the pent-up fluid into the subarachnoid space, where it may be absorbed. Krause<sup>108</sup> **drained directly the cavity of the ventricle into the subcutaneous tissue of the scalp** by means of a silver tube inserted through the cortex into the ventricle and held in place (in some cases for several months).

In the non-obstructive hydrocephalus, Frazier (*loc. cit.*) recommends the **establishment of a drainage tract into the pleural cavity**, which is a convenient and readily accessible reservoir.

Among other procedures the following may be mentioned: The experiments by Payr to effect a drainage by means of freely transplanted blood-vessels appear very promising, as the method establishes a direct

connection between the lateral ventricles and the longitudinal sinus. Heile<sup>109</sup> reports a case of internal hydrocephalus in which he implanted a rubber tube 5 mm. in diameter leading from the lower end of the spinal dural sac to the abdominal cavity in the triangle of Petit above the ilium, passing between the external and internal oblique muscles. In this case (a boy of eight) extraordinary improvement was obtained in the gait, while a previous puncture of the corpus callosum gave no relief. In another case, which proved to be one of hydrocephalus of the fourth ventricle, he diverted the excess of fluid into the intrapleural space by means of an implanted rubber tube. In order to reduce friction from the tube in the pleura, he slipped, over the lower end, a segment taken from a living jugular vein near by. In both cases the wounds healed in place without reaction. In the second case, choked disk, headache and vertigo entirely subsided. The benefit in the second case during five months to date, says the author, has surpassed anything yet realized in treatment.

Finally, Finkelnburg<sup>110</sup> recommends puncturing the motor area at a depth of 5 cm.

**Prognosis.**—The outlook is serious. Death usually occurs at an early age and most frequently from some intercurrent disease or from profound nutritional disturbances. In a few traumatic cases, the hydrocephalic fluid found a passage through the nasal fossæ, orbital cavity, mouth, ears, and thus evacuated externally until a spontaneous cure took place. Such cases, however, are very rare. That hydrocephalus may become arrested in its development is a well-known fact: the sutures become then ossified and the head ceases to grow large; the individual may live long, but the peculiar shape of the head remains unaltered. In some cases, months or years after the arrest of the pathological process, a recurrence with reformation of a large amount of fluid takes place.

## B. LATERAL VENTRICLES

In discussing symptomatic hydrocephalus mention was made of extensive ventricular exudation in serous meningitis. This occurrence is constant in the meningococcus form of cerebrospinal meningitis. In the latter, ependymal lesions are very frequent, from mere congestion to pus formation. In a recent contribution based on observations collected during the War since 1914, J. Cassade<sup>111</sup> considers the following possibilities: (1) acute congestive ependymitis and choroiditis; (2) acute suppurative ependymitis and choroiditis; (3) acute serous ependymitis and choroiditis with dilatation of the ventricles; (4) acute suppurative ependymitis and choroiditis with ventricular dilatation; (5) pyocephalia without basilar lesions.

When ependymitis develops in the course of cerebrospinal meningitis, the symptomatology of the latter assumes a different aspect. Somnolence is extreme and intelligence becomes cloudy. Headache is exceptionally severe and is accompanied by delirium. The limbs become rigid and sometimes tetanic. The emaciation is extreme. The cerebrospinal

fluid is diminished in quantity and is slightly yellowish in color. Treatment should consist of ventricular puncture followed by injection of **antimeningococcus serum**. Serotherapy by lumbar puncture is badly tolerated, as epileptiform convulsions have been observed.

### *Pyocephalia*

When the ventricular fluid becomes purulent, serotherapy cannot always be depended upon. This form of ependymitis and choroiditis is the most serious variety and presents a special clinical and pathological picture. It is known under the name of *pyocephalia*.

Three anatomical elements are to be considered here: (1) the suppurative ependymitis; (2) retention of the purulent fluid under high pressure which distends the ventricles; (3) isolation of the ventricles from the subarachnoid spaces.

Pyocephalia was mentioned by Netter and Debré, Haushalter, Riliet, Triboulet, Cushing and Slaven, and others, as an incidental complication. It was Chiray<sup>112</sup> who collected all the isolated data and, basing his conclusions on personal observations during the War, presented the subject in an elaborate manner as a nosological entity.

**Pathology.**—The meninges of the brain present irregularly distributed areas of infiltration along the blood-vessels and at the base. The pia-arachnoid is adherent to the cortex, and especially at the base in the pontine region cysts filled with turbid fluid are seen. The brain is enlarged and tense. The ventricles, especially the lateral, are enormously dilated; their walls are gelatinous, thick and covered with islets of pus. The choroid plexuses are covered with pus. The fluid in the ventricles is abundant, so that their walls are widely separated from each other. It is turbid and purulent. It is rich in fibrin, polynuclear cells and meningococci. All communications between the ventricular and extra-cerebral circulation of the cerebrospinal fluid are totally abolished. This explains the fact why, in such cases, lumbar punctures will give no assistance whatsoever in the determination of pyocephalia and why injections of serum by this route will not reach the diseased areas.

**Symptomatology.**—In the midst of apparent amelioration of the meningeal symptoms when treated with the antimeningococcus serum, suddenly or rapidly there is a recrudescence of the acute symptoms, viz., rigidity of the neck and spine, also fever. Serum reinjected apparently has no more its beneficial influence. A radical change then takes place in the patient's condition. Trophic disturbances are most striking: a diffuse muscular atrophy, dryness of the skin, various eruptions, bedsores and extreme emaciation are most conspicuous.

Psychic disturbances with somnolence and mental hebetude, vacant facies, immobility and occasional mild delirium, are all in evidence. Incontinence of urine and feces is frequent.

Motor disturbances consist of a paretic state of all extremities, some rigidity and tremor. Reflexes are all diminished or abolished.

Sensory disturbances consist of a generalized hyperesthesia. Some

deafness is present. The pupillary reflexes are sluggish, the papillæ show some venous stasis.

Respiration is frequently of Cheyne-Stokes' type. Pulse is either accelerated or depressed. The temperature is only slightly above normal.

The spinal fluid in the course of cerebrospinal meningitis is variable. Generally speaking, under the influence of serotherapy, the modification of the fluid runs parallel with the improvement of the patient. When the latter takes place, it becomes clear; the polynuclear cells gradually decrease and finally give place to lymphocytes; the meningococci gradually disappear.

When pyocephalia develops, in spite of the amelioration of the clinical symptoms, the spinal fluid does not change, its color and the cytological formula remain unaltered, also the meningococci do not reappear. Moreover, in some cases of pyocephalia, it is difficult to obtain the smallest quantity of fluid on lumbar puncture. When serum is injected, it fails to be absorbed, which can be seen from the fact that a lumbar puncture, a day or two later, brings forth a yellowish serum. It is evident that there is an obstacle to the penetration of the serum into the ventricles.

Chiray also observed the following interesting phenomenon, which he considered as pathognomonic of pyocephalia: If one-half of a cubic centimeter of antimeningococcus serum is injected into the patient's vein, one observes in ten to thirty seconds that his face becomes very red, while the lips and ears become purple; the conjunctivæ are congested and the eyes water; mental hebetude increases and the patient loses consciousness; the respiration becomes irregular and the pulse imperceptible. In four or five minutes the alarming symptoms disappear.

To sum up, pyocephalia presents three main characteristic features which are of diagnostic value, namely: the special clinical signs, the negative data concerning the spinal fluid, and finally, the so-called "reflex sign" of Chiray, which concerns the circulatory, respiratory, vasomotor and cerebral manifestations provoked by an intravenous injection of a very small dose of therapeutic serum.

**COURSE.**—The evolution of the symptoms lasts from two to five months. It may be interrupted by acute phases every two or three weeks; then the fever and rigidity become more pronounced. They leave the patient more and more fatigued. Gradually his state becomes aggravated and he succumbs in a state of total exhaustion and cachexia. The serum treatment is as a rule inefficacious.

**Treatment.**—Repeated lumbar punctures with spinal injections of meningococcus serum do not interfere with the fatal evolution of the disease. On the other hand, intraventricular injections of the serum, administered repeatedly and particularly early in the course of cerebrospinal meningitis, may give favorable results. Statistics show that in a few cases recovery was obtained (Netter, Triboulet, Cushing). The general impression is that in 20 per cent. recovery has been observed in cases in which the ventricular treatment was undertaken in the early stage of the disease.



*Ventricular Hemorrhage*

Hemorrhage in the brain may be extraventricular or intraventricular. In the latter case the blood may originate in the ventricle itself and produce a primary ventricular hemorrhage. In the first, the original seat of the hemorrhage is the tissue surrounding the ventricle and the ventricle itself is only secondarily involved. While the secondary hemorrhage is not an infrequent occurrence, the primary ventricular hemorrhage is not frequent.

A study of both forms presents such a uniformity in the anatomico-clinical aspects that their diagnostic value becomes self-evident.

**Pathology.**—A study of twelve cases under the author's observation permits the writer to draw a distinct picture.

From the time of Morgagni up to the present, the majority of observers believed that the choroid plexuses are the origin of primary ventricular hemorrhage. Degeneration, chronic inflammation, fatty changes, calcareous deposits, dilatation, all these conditions have been observed in the vessels of the plexuses. Thromboses, aneurysms, angiomatous tumors and cysticerci attached to the plexuses have been observed in a few cases (Broca). Serous cysts originating in the walls of the blood-vessels have been found in aged individuals, also in cases of atrophy of the brain (Wilks). Besides degenerative changes in the walls of the blood-vessels of the plexuses, especially in the intima, miliary aneurysms have also been found. Charcot and Bouchard, in 1868, announced that miliary aneurysms were the chief cause of cerebral hemorrhage, but subsequent investigations proved that whether the hemorrhage is produced by simple rupture of the vessel wall or of a miliary aneurysm, in both cases profound changes of some or of all layers of the wall are always present.

The seat of the primary interventricular hemorrhage may be either in one or both lateral ventricles; the right ventricle seems to be the predominant seat.

The brain tissue in the immediate vicinity of the hemorrhage suffers destruction. Pushing outward the remaining cortical substance, the hemorrhage exercises also considerable pressure on the opposite hemisphere and displaces it.

In the secondary ventricular hemorrhages the original rupture of the blood-vessels occurs mostly in the internal capsule. The same pathological changes of the blood-vessels mentioned above are found here.

**Differential Clinical Features.**—In 5 cases of the primary and in 7 cases of the secondary ventricular hemorrhage the following manifestations were observed. In the primary form there were: sudden onset; the most profound coma from the very beginning; convulsions more marked on the side opposite to the lesion than on the same side in the unilateral cases, and on the side opposite to the seat of the largest hemorrhage in the bilateral cases; finally, absence of marked paralysis. These four symptoms were uniformly present in all the five cases at the time when the attack was ushered in.

The most striking phenomenon was the absence of true paralysis and of rigidity. At first, similarly to ordinary cerebral hemorrhage, the sudden loss of power was evident, but subsequently during the patient's short life the usual rigidity and contracture did not appear. The reflexes also presented certain peculiarities: the patellar tendon

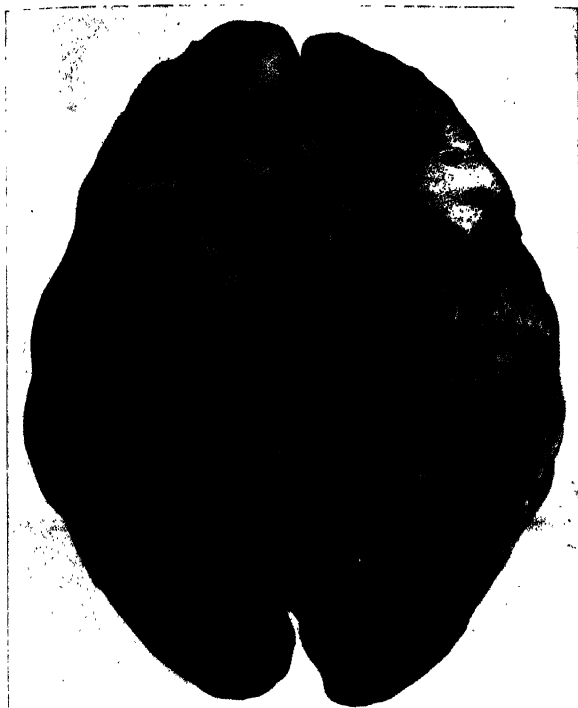


FIG. 9.—PRIMARY INTRAVENTRICULAR HEMORRHAGE (IN LATERAL CORNU ON RIGHT).

Note deviation of opposite side. Case operated upon. (Gordon, Courtesy *Archives of Internal Medicine*.)

on the affected side was not especially increased, although it was greater than on the normal side; ankle clonus was absent; the toe phenomenon was also absent.

In the cases of secondary ventricular hemorrhages, the already existing paralysis and contracture became markedly accentuated at the time the ventricles were invaded. The abnormal reflexes which are usually present in hemiplegias were manifest here.

The onset in the primary cases was also special: in the majority of the cases there was no special premonitory symptom (objective or subjective).

The character and duration of the coma are of interest. In the primary hemorrhage coma appeared at the commencement of the seizure and remained complete throughout the short life. In the secondary ventricular hemorrhage the coma was also present with the irruption of the blood into the ventricle. Therefore, the mere existence of unconsciousness is of little value in differential diagnosis. It is the sudden onset of profound coma without preceding hemiplegia that will determine the diagnosis of a primary hemorrhage in the ventricle.

**Prognosis.**—The termination is also somewhat different in both varieties of hemorrhage. In the cases of the primary variety, life persisted from six to twenty-four days. In the series of the secondary variety, death followed but a few hours after the inundation of the ventricles. It seems, therefore, that the fatal issue is less rapid in the primary than in the secondary variety of ventricular hemorrhage.

**Treatment.**—In 3 out of the 5 cases of primary ventricular hemorrhage, there was displacement of the brain tissue to the opposite side, and consequently the possibility of the comatose state as due to sudden undue pressure on the normal side of the brain appeared to be highly plausible. Such a finding in one case suggested **surgical intervention** with the object of relieving the intracranial pressure on the sound side. An attempt was made in one case for a decompressive operation. Although the patient did not recover eventually, nevertheless the duration of her life was prolonged twenty-four days. Immediately after the operation there was a decided improvement in her respiration, in response to external stimulation, in the cardiac action. For several days she could open her eyes voluntarily; she could be fed more readily than before and she could swallow. The improvement obtained was undoubtedly due to the relief of intracranial pressure. Unfortunately, the operation was consented to only on the fifth day after the apoplectic seizure, viz., after five days of a comatose state. It is, therefore, highly probable that if a decompressive operation were done promptly on the sound side, favorable results might have been expected.

## XII. BASE OF THE BRAIN

The presence of the cranial nerves at the base of the brain renders the symptomatology of lesions over that surface quite complex. There will be symptoms referable to both the nerve tracts on their passageway from above downward and to the cranial nerves. The cranial nerve symptoms depend upon the nerve or nerves involved, but in almost all cases there will be one common manifestation, viz., crossed or alternate paralysis. The latter consists of a hemiplegia affecting the side of the body opposite to the side of the lesion and of a palsy of one or more cranial nerves on the side of the lesion. It finds its expla-

nation in the fact that a tumor or any lesion lying on one side involves the motor and sensory fibers above their decussation, also the superficial origin of the cranial nerves, which do not undergo decussation, at the base of the brain. Should the lesion occupy the median line and thus produce bilateral pressure or irritation, the paralysis will be bilateral. Tumors which originate in the bones or in the cerebral membranes at the base, affect at first and for some time afterwards the cranial nerves exclusively, so that crossed hemiplegia will develop late, when the neoplasm in its progressive course will involve the cerebral tissue.

#### A. EXTREME ANTERIOR PORTION

Tumors of the extreme anterior portion of the basal surface of the brain, viz., of the inferior surface of the frontal lobes, will give rise to olfactory and visual disturbance because of the pressure in that region of the first two pairs of cranial nerves.

When the olfactory nerve is involved, loss or impairment of the sense of smell (anosmia) is the prominent symptom. As the taste is dependent to a large extent on the integrity of smell, the former will be affected when anosmia is present. When the olfactory nerve is in a state of irritation, hallucinations of smell (parosmia) may occur. (*See also the section on Hippocampus.*) Very recently it has been advanced by F. Kennedy that the tumor or abscesses involving the inferior or orbital surfaces of the frontal lobe produce homolateral retrobulbar optic neuritis, central scotoma and optic atrophy, and contralateral choked disk. These findings may be of diagnostic value.

#### B. INTERPEDUNCULAR REGION

The involvement of the interpeduncular region, viz., the space between the longitudinal fissure in front and the crura cerebri behind, is frequently associated with hypophyseal manifestations. Tumors of the hypophysis, besides the acusticus tumor, constitute the most frequent localizations at the base of the brain. Tumors localized in the lower portion of the third ventricle through the pressure against the base will give place to hypophyseal manifestations, or more correctly, "the infundibular syndrome" described in the section on the third ventricle.

Aneurysms of basal cerebral arteries are not rare. In all varieties of lesions in the interpeduncular space symptoms referable to the disturbed function of the pituitary body will always be present. In view of the close proximity of the chiasma, bitemporal hemianopsia is invariably the most conspicuous symptom.

#### C. HYPOPHYSEAL REGION

A brief review of conditions occurring in diseases of the hypophysis cerebri may be appropriate.

Hemianopsia.) Optic neuritis and optic atrophy are not infrequent. If the tumor extends posteriorly so as to irritate or press against the crura cerebri, symptoms of motor or sensory character with change of reflexes will be manifest (hemiplegia, etc.). When the tumor reaches the pons, involvement of the third and fourth nerves will take place.



FIG. 11.—TUMOR OF HYPOPHYSIS.

Crura compressed; pons and medulla displaced. (Gordon, *Courtesy of Johns Hopkins Hospital, Bulletin of Internal Medicine.*)

When the hypophyseal tumor after destroying the sella turcica presses on the orbital cavity, exophthalmos will occur. In one of the author's cases there was a total olfactory loss, and there was no reaction to even the most intense odors, such as that of ammonia placed close to the nose. At autopsy the pituitary tumor was found extending downward and after destroying the sella turcica penetrated, through the opening thus formed, the posterior nasal spaces. (Gordon.<sup>118</sup>)

## D. THE PONS

The pons contains motor and sensory tracts going to and coming from the brain. Through the middle cerebellar peduncles, it is connected with the cerebellum. A number of cranial nerves appear at the borders of the pons on their way from their respective nuclei in the medulla. Consequently the symptomatology of pontine lesions must be complex and vary from one case to another, according to the part of the pons involved.

**Pathology of Diseases of the Pons.**—*Hemorrhagic foci* are usually located in the median line. They may spread downward and forward. They are rare. *Softening* is quite frequent and it is due to thrombosis of the basilar artery. Softening sometimes occupies the largest part of the pons; sometimes it is on one side and sometimes on both. In aged people the disintegration of the pontine tissue occurs in small areas which sometimes are multiple. *Tumors* are not frequent. Tubercles are the most frequent. Next in frequency are gummata. Gliomata may also occur. Cysts, cancer, abscesses are very rare. (For the state of the nervous tissue see section on Apoplexy.)

**Symptomatology.**—(1) **HEMORRHAGE.**—The onset is sudden and loss of consciousness especially in large hemorrhages is always the first symptom. In small hemorrhages there may be no loss of consciousness. When the patient has regained consciousness, one will observe the following symptoms: contracture of the extremities accompanied by generalized convulsions or unilateral epileptiform convulsions; conjugate deviation of the eyes and head, crossed paralysis.

The conjugate deviation presents special features. If the pontine lesion is destructive and leads to a unilateral paralysis, the eyes will be turned toward the paralyzed side. If it is irritative and leads to unilateral convulsions, the eyes will be turned away from the affected side.

Myosis, dysarthria and dysphagia are quite frequently observed in pontine hemorrhage. Death occurs from cardiac or respiratory paralysis.

Crossed paralysis will be discussed later.

(2) **SOFTENING.**—The onset is rarely sudden, more frequently slow. In the latter case it is preceded by prodromal symptoms, such as headache, vertigo and paresthesia in the limbs which are to be affected. Crossed hemiplegia is the usual result. Dysarthria and dysphagia are quite frequent. In thrombosis of the basilar artery, in addition to the above symptoms, there are also somnolence, optic neuritis and sometimes delirium.

(3) **TUMORS.**—They may originate in the pons or in the vicinity at the base, most frequently in the pontocerebellar angle. Similar to cerebral tumors, pontine neoplasms present general and focal symptoms. The first are: headache, vomiting, vertigo, insomnia, optic neuritis. The headache which is frequently occipital may be accompanied by stiffness of the neck. Percussion of the occiput and of the first cervical spinous process may be painful. Optic neuritis appears late or in the terminal

stage of the disease. The focal symptoms are: **crossed paralysis**, which is slow in development. A very frequent occurrence is subjective pain in the paralyzed muscles of the limbs and face (when the latter is involved). The cranial nerves are usually involved. In some exceptional cases, the nerves alone are affected, in others the nerves are intact and there is only contralateral paralysis of the limbs. This possibility will occur only in lesions of the upper part of the pons. If the tumor is so extensive as to involve the medulla, cerebellum or other neighboring tissue, the symptomatology will be more complex: unilateral paralysis of the palate, vocal cords, tongue (ninth, tenth, eleventh and twelfth nerves). Polyuria, disturbances of respiration and of heart beat are indications of bulbar involvement. Vertigo, titubation, show involvement of cerebellar peduncles. Diminution of central visual acuity is an indication that the anterior quadrigeminal bodies are involved; deafness is an indication that the posterior quadrigeminal bodies are involved. As in hemorrhage and softening, dysphagia and dysarthria are also present and even quite frequent in tumors. Dysphagia is caused by an involvement of the medulla, dysarthria by involvement of the central fibers of the hypoglossus. Anarthria implies a bilateral lesion in the pons.

Ataxia is frequent in pontine lesions. It is usually unilateral. It is probably due to the implication of the fillet, which produces sensory disturbances. When the gait and station are disturbed, the cerebellum or its peduncles are probably involved.

**CROSSED PARALYSIS.**—From the foregoing remarks it can be seen that crossed paralysis is a common feature in diseases of the pons. The paralysis may be motor or sensory, but most frequently combined. There are two varieties of crossed paralysis: *superior* and *inferior*.

(a) The *superior crossed paralysis* is due to a lesion above the upper border of the pons or else involves simultaneously also the upper portion of the pons.

In the first case we deal with the *peduncular syndrome*; in the second case with *pedunculopontine syndrome*. Both are known as *Weber's syndrome*.

If the lesion is above the pons and localized in the *anterior* portion of the peduncle, which is *motor* and which is separated by the locus niger from the posterior (upper) portion, which is sensory, the resulting crossed hemiplegia will be exclusively motor. In such cases it is difficult to differentiate the condition from other cerebral hemiplegias. In the pedunculopontine variety of Weber's syndrome, there is a crossed hemiplegia involving the arm, leg and face (the facial paralysis is of the cerebral type, viz., affecting only the lower half of the face, but there is also a palsy of the third nerve on the side of the lesion (the latter palsy may be complete or partial). When the lesion implicates the inner four-fifths of the foot of the crus and destroys all the cortico-nuclear pathways, there will be present, in addition to the crossed paralysis of the third nerve, also conjugate deviation of the head and eyes on the hemiplegic side. In some cases instead of hemiplegia there is hemitremor of the choreo-athetotic type. This peduncular crossed paralysis

is known under the name of *Benedikt's syndrome*. The lesion is probably in the tegmentum of the crus.

(b) The *inferior crossed paralysis* is known under the name of *Milard-Gubler's syndrome*. It is characterized by a paralysis of the arm and leg on the side opposite to the lesion, and of the sixth and seventh nerves on the side of the lesion. The facial paralysis is of the peripheral type (affecting the entire side of the face and electrical reactions of degeneration are present). If the lesion is above the lower border of the pons, there will be only hemiplegia but no involvement of the sixth or seventh nerve.

Other nerves may be involved in pontine lesions. If the fifth nerve is affected, there will be disturbances of tactile sensibility over the area of distribution of this nerve on the same side and hemiplegia on the opposite side. If the eighth nerve is affected by the pontine lesion, there will be impairment of hearing on the same side and hemiplegia on the opposite side.

Under the name of *Foville's syndrome* is known a paralysis of associated movements of the eyes; the internal rectus (third nerve) of one side and the external rectus of the other side (sixth nerve) no longer functionate in their synergic movements. Pathologically there is either an irritating or a paralyzing lesion of the corticonuclear pathway connecting the cortex with oculomotor nuclei, or a lesion of the fibers connecting Deiters' nucleus with the oculomotor nuclei, or else a lesion of the fibers connecting the nucleus of the third of one side with the nucleus of the sixth of the other side, fibers which pass through the posterior longitudinal bundle.

**HEMIANESTHESIA.**—The *crossed paralysis* which is so characteristic of pontine lesions may be, as intimated above, not only motor but also sensory.

When the lesion, instead of being localized in the anterior portions, affects the posterior portions (tegmentum) of the crura and pons, and especially their reticulate substance and the mesial fillet, the result will be *hemianesthesia* on the side opposite to the lesion.

*Peduncular and pontine hemianesthesia* differs from cortical, capsular or thalamic sensory disturbance in that it is very frequently of *syringomyelic type*. In view of the fact that tactile sensibility and the sense of position are controlled by the mesial fillet, while the sensations of pain and temperature are controlled by the reticulated substance, all variations of hemianesthesia may be encountered in lesions of the tegmentum. All depends upon the exact seat of the lesion.

Another characteristic feature of the hemianesthesia is that it decreases in intensity from the periphery to the root of the limb.

When the lesion of the sensory pathway involves also the nuclei of the nerves, the result will be *crossed hemianesthesia*. In this variety of hemianesthesia the sensory disturbance occupies the half of the face on the side of the lesion, because of an involvement of the radicular fibers or of the long descending branch of the fifth nerve. There will be a *global anesthesia* of half of the face, tongue, palate and pharynx on the



same side and the hemianesthesia of the arm and leg of syringomyelic type on the other side. Frequently paralysis of the masticator muscles is associated.

Purely sensory crossed paralysis is rare. More frequently the latter is associated with motor paralysis on the same side. The lesion in such cases affects both the anterior and posterior portions of the pedunculo-pontine region. In such cases the hemiplegia and hemianesthesia are accompanied by cerebellar symptoms, anesthesia of the face, paralysis of the face and of eye muscles, auditory disturbances—because of the involvement of the various nuclei or of their efferent fibers. We are then in presence of a *crossed sensorimotor paralysis*.

**Diagnosis in Pontine Lesions.**—PONTINE HEMORRHAGE will be differentiated from intracranial hemorrhage in general mainly by the presence of alternate paralysis, but also by convulsions and hyperesthesia of the affected limbs. The conjugate deviation of the head and eyes presents a very important diagnostic sign. Landouzy put down the following rule:

	<i>Pontine lesion</i>	<i>Cerebral lesion</i>
In Paralysis	{ Eyes turned toward the paralyzed side.	{ Eyes turned toward the non-paralyzed side.
In Convulsions	{ Eyes turned toward the unaffected side.	{ Eyes turned toward the affected side.

SOFTENING is recognized by prodromal symptoms.

TUMORS are of slow and progressive evolution. *Intrapontine tumors* commence often by associative progressive paralysis of the lateral movements of the eyes, predominant on the side of the lesion. It is accompanied by motor and sensory disturbances on the side opposite the tumor. Implication of the auditory nerve is a late symptom.

*Extrapontine tumors* are mostly tumors of the *pontocerebellar angle*. They are also called acoustic tumors. Neoplasms situated in the angle formed by the cerebellum and pons present symptoms referable to the cerebellum, to the tracts in the pons and to the cranial nerves which emerge in close proximity. They most frequently begin with unilateral auditory disturbances which may for a long time escape the notice of the patient himself. Hypoacusia and vertigo with tinnitus are often first signs of localization. Objectively the ear findings are normal. Gradually complete deafness develops. Although the facial nerve is adjacent to the auditory, nevertheless the involvement of the first is not an early sign. So it is with the sixth nerve.

As the course is slow but progressive, new symptoms are gradually being added, so that the diagnosis in the first period of the disease is somewhat obscure. Sometimes for weeks and months there will be only general manifestations of intracranial pressure, such as headache, vomiting and vertigo, and with the exception of the hypoacusia there are practically no localizing symptoms. The latter develop slowly.

As the eighth, seventh, sixth and fifth nerves are most frequently

involved, the following symptoms will be observed: Impairment of hearing on the side of the tumor which usually leads to total deafness (eighth nerve), also vertigo with a tendency to fall toward the affected side—the latter may occur also in paroxysms according to Ziehen; facial paralysis of the peripheral type; anesthesia of certain portions of the face on the side of the tumor including the cornea (fifth nerve); paresis or paralysis of the external rectus muscle of the eye on the affected side, hence internal strabismus (sixth nerve).

*Compression of the pons itself* causes a contralateral paralysis of the limbs and corneal areflexia and paresis of associated movements of the eyes (*Blicklähmung*) when the patient turns his head to the side of the tumor. Dysarthria and dysphagia are frequently present. As the motor and sensory pathways pass through the pons, paresis or paralysis, anesthetics or analgesias or else paresthesias, changes of reflexes will be observed. Sensory disturbances are, as a rule, not frequent, and, if present, they are very slight. Motor disturbances are also not pronounced, but changes in reflexes are quite conspicuous. The knee-jerk may be increased on the opposite side and not infrequently diminished on the side of the tumor. The toe phenomenon and ankle clonus may be present on the side of the increased knee-jerk.

Next in diagnostic importance stand the manifestations referable to the *cerebellum with its peduncles*. They are briefly as follows: Ataxic gait, with a tendency to walk to the side of the lesion; ataxia of the limbs on the side of the lesion, adiadokokinesis (unilateral); inclination of the head on the affected side. A detailed discussion of these symptoms will be found in the section on the Cerebellum.

Besides the above-mentioned disturbances of the ocular muscles, there may be also present nystagmus and engorgement of the veins, with edema of the papilla, but the latter symptoms as a rule do not make their appearance in the beginning of the case. Sicard and Roger<sup>118</sup> have recently reported a symptom which they could not find mentioned by any previous author. They observed in a case of pontocerebellar tumor paroxysmal crises of Stokes-Adams syndrome. The latter, they believe, is not the result of cerebral hypertension, but the consequence of a compression of the medulla and of the tenth and eleventh nerves by the tumor. The diagnosis of a pontocerebellar tumor is based chiefly on symptoms of compression of the cranial nerves at the base. As the first manifestation occurs ordinarily in the domain of the eighth nerve, the condition of the latter must be carefully analyzed. In making a differential diagnosis the slowness of development of symptoms must be borne in mind, and therefore special attention should be directed toward the minute details as to cranial nerves, to disturbances of synergic action of the upper and lower limbs, to the state of reflexes, to the gait and station. An examination of this type will invariably reveal a predominance of symptoms on one or the other side.

In differentiating the pontocerebellar (extrapontine) from intrapontine tumors, one must not ignore the fact that in the former the

papillitis (choked disk), when it occurs, is usually very pronounced, while in the latter it is usually absent. Also the disturbances of the acoustic part of the eighth nerve are constant, very deep and conspicuous in the former, while they are exceptional in the latter. The distinction between extrapontine and intrapontine tumors is of great importance, as surgical intervention depends on it. While the latter are not amenable to surgical treatment, in the former a decompressive operation with a possible removal of the neoplasm may be attempted.

### **XIII. MEDULLA OBLONGATA**

The medulla is connected with the higher centers and the peripheral nervous system. Besides, it functionates as an independent center of the greatest importance.

It contains the pyramidal system which is the chief path of the volitional motor system between the cortex and the anterior cornua of the spinal cord. It contains the paths of cutaneous and general sensibility. Both pathways decussate in the medulla so that those of one half of the body are situated in the opposite half of the medulla.

The posterior columns of the spinal cord end in special nuclei of the medulla, which in their turn send out tracts for connection with cerebral and cerebellar centers. The direct cerebellar tract of the cord goes through the inferior cerebellar peduncles to the cerebellum.

As an independent center the medulla controls and regulates most important functions on which the maintenance of life depends. The last eight pairs of cranial nerves originate in the medulla, and the third and fourth nerves are connected with the nuclei of the sixth nerve through the posterior longitudinal bundle. It is evident that the medulla contains centers of reflex coördinations of the most complex functions related to the distribution of the largest majority of the cranial nerves, so that a lesion of the medulla causes sudden or rapid cessation of associated movements. The various afferent and efferent nerves concerned in the mechanism of the associated movements play an important rôle in coördinate synergy of some muscles, in the production of articulate speech (for example, bulbar paralysis), in emotional expressions, in respiratory movements, in the action of the heart, in the state of blood-pressure, in the arterial tonus (vasomotor center).

Apart from all these special functions of the medulla, there is another one discovered by Claude Bernard, viz., the influence of lesions of the floor of the fourth ventricle on the processes of assimilation and excretion. He found that a puncture of the fourth ventricle, near the nuclei of the tenth nerve, produced a glycosuria. The explanation given by Cyon is that the lesion of the medulla causes disturbance of the circulation and glycogenic function of the liver, and that the formation and excretion of sugar is a secondary result of the vasomotor paralysis of the liver.

## A. ACUTE SUPERIOR POLIO-ENCEPHALITIS

Anatomically it consists of an inflammation with hemorrhages in the gray matter of the aqueduct of Sylvius. The nuclei of the third and fourth nerves, also the fibers emerging from them, are therefore the main seat of the lesion. Diseased condition of the blood-vessels (arteriosclerosis or syphilitic endo-arteritis), miliary aneurysms, especially under the influence of increased blood-pressure, cause hemorrhage with destruction of nerve tissue. Severe traumatism on the back of the head can also give rise to hemorrhages in the region of the upper bulbar centers. Finally inflammatory conditions may be observed in intoxications and infectious processes. Chronic alcoholism is the most frequent cause. Alimentary intoxications (fish, meat, etc.), carbonic acid, sulphuric acid, are sometimes followed by superior polio-encephalitis. Microscopically are seen dilated blood-vessels, perivascular infiltration, small hemorrhages, degeneration of the nerve-fibers and ganglion cells. Sometimes these pathological processes extend forward into the floor of the third ventricle and backward into the fourth ventricle.

**Symptomatology.**—The onset is acute. As a rule, headache, especially in the lower occipital region, and vertigo precede for a few days the onset of the disease, which is sudden and apoplectiform in character. Consciousness may or may not be lost. Palsies of the eye muscles rapidly develop. Most of the time both eyes are involved, but the degree of palsy is unequal. Sometimes an associated paralysis is observed: either both external recti or both internal recti are affected. Ptosis is not frequent. Wernicke, whose name is attached to the disease, claims that the sphincter of the iris is never involved, but this statement is too absolute, as the author has records of two cases with palsy of this sphincter. Optic neuritis and nystagmus may occur.

In addition to the ocular disturbances, which are the characteristic feature of the disease, other symptoms are not infrequently observed. The extension of the inflammatory process from the gray to the white matter of the pons and medulla will cause ataxia, unilateral paralysis of the extremities, disturbance of speech (*see* Anarthria), exaggeration or abolition of the tendon reflexes; disturbances of deglutition and of mastication may be met with.

As the inflammation may become diffuse and be ascending or descending or both, the cerebral as well as spinal symptoms may be associated. Polio-encephalitis, superior and inferior, and poliomyelitis may be combined (Polio-encephalomyelitis).

**Course, Duration and Prognosis.**—The evolution of the symptoms is rapid. In the majority of cases the duration is from eight to fourteen days, although in one case it lasted sixteen weeks. Recovery was reported in a few cases. In one of the author's cases the palsy of the third and fourth nerves had been in existence two and one-half years. The patient is still living. She was addicted to the use of alcohol at the time the disease developed. The onset of the latter was apoplectiform with loss of consciousness. In another case, a child of ten months,

there was also loss of consciousness with involvement of the third, fourth and sixth nerves simultaneously. The child is now three years old and the nerve palsy has quite improved. The condition was preceded by attacks of coughing for a period of four to five days, evidently of infectious nature. In both cases the paralysis was bilateral, but unequally distributed to various muscles of the eye globes.

**Treatment.**—The general symptoms may be relieved by the usual medications. **Bleeding, purgatives and diaphoretics** may be tried. **Iodids** may be of some help.

## B. ACUTE INFERIOR POLIO-ENCEPHALITIS

### (*Acute Bulbar Palsy*)

The character of the lesion, the causes of it, the pathological state of the tissue, the onset and the general symptoms are all identical with those in the superior variety discussed in the previous chapter. The difference lies only in the localization. Here all other nuclei, except those of the third and fourth, are involved or only some of them.

**Symptomatology.**—Whether the disease is due to a hemorrhage, embolism and thrombosis of the basilar trunk, or to an extension of an acute poliomyelitic process to the bulbar nuclei, the onset is more or less sudden, with or without loss of consciousness, and the special bulbar symptoms, viz., dysarthria, dysphagia, palsy of the lower half of the face, etc., appear immediately. The picture is that of labioglossopharyngeal paralysis. The tongue, lips, palate, are paralyzed.

The dysarthric disturbances in speech are especially characteristic. The latter is thick, hoarse and aphonic. The food is regurgitated through the nostrils and sometimes into the larynx, causing a cough. The paralysis of the soft palate, the loss of pharyngeal and palatal reflexes, difficulty of deglutition, threaten the patient with suffocation. The paralysis of the face is striking; it is of the peripheral type. Facial paralysis is frequently followed by paralysis of the sixth nerve on the same side. Trismus is, according to Joffroy, a not infrequent symptom because of the involvement of one of the motor nuclei of the fifth nerve, so that the patient has difficulty in masticating.

If the lesion extends upward to the crura, the central paths for the limbs and for the seventh, tenth and twelfth nerves in unilateral lesions will be affected above their decussations; the symptoms will be: oculomotor paralysis on the side of the lesion and a supranuclear paralysis of the above bulbar nerves and of the limbs on the opposite side (see Weber's Syndrome). It is known under the name of *hemiplegia alternans superior*. When the nucleus of the seventh nerve and the pyramidal tract at the same level are involved, the result will be a facial paralysis on the side of the lesion and paralysis of the extremities on the opposite side. It is known as *hemiplegia alternans inferior*. In the latter case there is often a paralysis of the sixth nerve on the same side. When the deeper structures of the medulla are involved so that

the nuclei of the tenth, eleventh and twelfth nerves and their motor roots become invaded on one side, the result will be paralysis of the tongue, soft palate and the muscles of deglutition on the side of the lesion, also paralysis of the extremities on the opposite side. (The pyramidal tracts decussate lower down.)

It may happen that the lesion (softening or inflammation) involves the nuclei of the bulbar nerves on one side and passes the middle line



FIG. 12.—CASE OF BULBAR PALSY, WITH INVOLVEMENT OF SEVENTH, TENTH AND TWELFTH NERVES.

so that the motor tracts on both sides are involved. We then have a unilateral paralysis of bulbar nuclei and bilateral paralysis of the four extremities. The paralysis of the parts innervated by the bulbar nerves presents special characteristics: similarly to the flaccid paralysis caused by poliomyelitis, a lesion of the bulbar nuclei causes also a flaccid paralysis. Moreover, just as in the former the reflex irritability is diminished, in the latter reflex irritability is abolished in the muscles of the face, tongue, pharynx and larynx. The same may be said with

regard to progressive atrophy, fibrillary contractions and reactions of degeneration. The acute bulbar nuclei paralysis is, therefore, in all objective respects identical with acute poliomyelitis, with this difference, however, that in the latter the lesion is in the cells of the anterior horns, in the former in the cells of the bulbar nuclei.

Similarly to the motor pyramidal tracts, the sensory tracts also undergo decussation, but in the higher parts of the medulla, so that the localization of the sensory disturbances on the side of the lesion or on the opposite side depends upon the seat of the lesion above or below the decussation. Thus we may have, for example, a crossed hemianesthesia with sensory disturbances on the face, in the mouth and in the pharynx, on the side of the lesion (fifth nerve). Tracts conducting all varieties of superficial and deep sensibilities pass through the deeper layers of the medulla. Consequently, according to the seat of the lesion, there may be all varieties of sensory disorders. A lesion, for example, in the higher portions of the medulla causes loss or diminution of the deep sensibilities on the opposite side; a lesion in the lower portions causes a disturbance of the deep sensations on the same side. Sensory dissociation of syringomyelitic type may be observed in lateral bulbar lesions on the opposite side. Brown-Séquard's type may also occur in unilateral spinal lesions. *Ataxia* will be present especially when the deep sensibility is involved. It is especially evident when the restiform bodies are involved. The special senses are rarely involved except when the eighth nerve is directly affected.

The medulla oblongata contains centers for the *vegetative functions* of the body. Thus in lesions of the medulla we may observe disturbances of respiration (Cheyne-Stokes type), of circulation (irregularity of pulse), of the temperature of the body, of vasomotor apparatus (secretion of perspiration), of assimilation and excretion (glycosuria and albuminuria), disturbances of the function of the sympathetic system by affecting the connections of the latter with the medulla (Horner's syndrome: ptosis, enophthalmos and myosis).

**Termination and Prognosis.**—In a large number of cases acute bulbar paralysis lasts from two to four days. If the acute symptoms subside and the patient survives, he is nevertheless constantly threatened with suffocation and aspiration pneumonia through the paralysis of deglutition. In exceptional cases great improvement may follow, probably because of absorption of the hemorrhages. In such cases atrophy will persist in the involved parts innervated by the diseased nuclei (atrophy of the tongue, etc.). In very mild inflammatory processes, complete recovery may take place.

**Treatment.**—**Revulsion, counterirritation on the neck, bleeding, iodids, maintenance of nutrition by artificial feeding** (stomach or rectum), **galvanism** applied to the neck, are all the means in our possession.

## C. CHRONIC SUPERIOR POLIO-ENCEPHALITIS

*(Progressive Nuclear Ophthalmoplegia)*

The disease is characterized by a slow but progressive paralysis of the muscles of the eye. It occurs in infections, intoxications, syphilis, also sometimes in the course of organic nervous diseases, viz., disseminated sclerosis, tabes, paresis. Pathologically it consists of an atrophy of the motor nuclei of the eye. Chromatolysis with formation of vacuoles and later disappearance of cells are the usual findings. Secondly, the roots emanating from the nuclei, the nerves themselves and the muscles innervated by the latter undergo degeneration. In some cases the nuclei of all the motor nerves of the eye are affected, in others only the nucleus of the third nerve is diseased.

**Symptoms.**—The onset is insidious. While there is no constancy in the order of involvement of individual ocular muscles, nevertheless ptosis and diplopia are the first symptoms in the majority of cases. As at the beginning the palsy is not complete; movements of the eye globe in certain directions are yet possible, but only after an effort. The facies of the patient is characteristic. As the upper eyelids are lowered, he holds his head thrown backward to be able to see objects; the forehead is wrinkled, as the frontal muscles are trying to raise the palsied eyelids. The movements of the eyes depend upon the muscles involved. In an advanced stage of the disease the eyes become immobile, and in order to see on the right or on the left, the head must be turned. In such cases the pupil no longer reacts to light or accommodation.

**Course and Prognosis.**—When the lesion remains confined to the ocular nuclei, the disease may last an indefinite number of years. It may begin on one side and remain confined to the same side. When it has a descending course and becomes complicated by an inferior polio-encephalitis, death may ensue in a very short time.

**Treatment.**—Antiluetic remedies may be tried. The disease is incurable.

## D. CHRONIC INFERIOR POLIO-ENCEPHALITIS

*(Chronic Bulbar Palsy: Labioglossolaryngeal Paralysis)*

The disease is characterized by a progressive paralysis of the muscles of the lips, tongue, pharynx and larynx. As a rule, it is observed in middle age and only exceptionally in childhood. Syphilis, fatigue, Bright's disease, traumatism, overexertion in certain occupations (glass blowing, blowing musical instruments) have been reported in the histories of some patients as etiological factors. The disease has also been observed in the course of amyotrophic lateral sclerosis, tabes, multiple sclerosis and syringomyelia.

Pathologically the affection consists of a primary and progressive



degeneration of the nuclei of origin of the cranial nerves situated in the lower half of the medulla, viz., those of the seventh, fifth (motor portion), ninth, tenth, eleventh and twelfth pairs. The alterations most marked are found in the nucleus of the twelfth nerve. They consist of diminution or disappearance of the chromophilic substance of the cells, of appearance of pigment within the cells, of displacement or disappearance of the nucleus, finally of atrophy of all the prolongations of the cells. Instead of wasted ganglion cells and the network of nerve fibers, there appear proliferation of neuroglia fibers and thickening of the vessel walls, but without any decided inflammatory changes. The nerve-roots emanating from the nuclei, the peripheral nerve fibers down to the muscles including the latter, all undergo atrophy. As to the participation of the white matter of the medulla, all writers are not agreed. Some claim (Raymond, Leyden, Dejerine) that the labioglossolaryngeal paralysis of Duchenne is not an autonomous disease, but is almost always followed by an involvement of the pyramidal fibers to constitute amyotrophic lateral sclerosis. In the ascending course of the latter disease, bulbar symptoms almost invariably appear, but there is also a form in which the disease begins with labioglossolaryngeal palsy.

**Symptomatology.**—The *onset* is insidious and slow. There is usually a brief prodromal stage during which the patient complains of pain in the neck and a numbness of the pharynx. Gradually the lips, larynx and the tongue become paralyzed. The *tongue* particularly is affected first in the majority of cases. At the beginning there is only a weakness in the movements of the tongue, but it keeps on increasing until complete immobility is established. The letters that require the coöperation of the tongue are imperfectly pronounced. The speech is, therefore, impaired (dysarthria). Muscular wasting and paralysis go hand in hand. The tongue is flat, diminished in size and presents fine fibrillary contractions, also reactions of degeneration. In an advanced stage the atrophy of the tongue is very marked; it then presents a depression and on palpation it is very soft. It can be moved with difficulty. It lies limp in the mouth and displays fibrillary contractions. The speech disturbances at first consist of difficulty in uttering lingual sounds, but afterward labial sounds are more and more affected. Finally, the speech becomes impossible (anarthria).

The weakness of the muscles of the *larynx* and paralysis of the *vocal cords*, paralysis of the *palate*, all contribute to disturbances not only of the voice but also of phonation. At first there is hoarseness, then loss of tone in the voice, finally the patient is unable to emit even a sound (aphonia).

The *lips* follow the tongue. It is the orbicularis muscle that is first affected, but soon other muscles suffer. The atrophy and paralysis of the lips interfere with the pronunciation of labial letters, with the act of blowing, whistling and laughing. Reactions of degeneration appear early. The lips become immobile, the mouth remains open and the saliva is continuously dribbling. When the *pharynx* is paralyzed, the food is likely to fall into the larynx, as deglutition is very difficult. The

patient is threatened with suffocation. The paralysis of the larynx increases the danger: the glottis being open, the food easily falls into the larynx.

The *facial muscles* are wasted in the lower half of the face and at the same time the muscles of the forehead and the eyelids, as a rule, remain intact.

The *facies* in a well-developed case is quite characteristic: it is rigid, wrinkled and emaciated; the mouth is open and its corners droop, the lower lip hangs down, the saliva dribbles; in attempts to laugh or cry the mouth is drawn outwards. The entire condition gives the impression of a stupid and crying face, but the expression of the eyes shows total integrity of intelligence.

The *muscular atrophy* and the state of *reflexes* deserve special mention. In the tongue and in the muscles of the lips reactions of degeneration set in early, but in all other muscles involved there is only diminution of electrical contractility for a long time.

The reflexes of the lower extremities are frequently increased. There is also exaggeration of reflexes in the masseter muscles. This fact shows the close relation of bulbar palsy to amyotrophic lateral sclerosis. The reflex irritability of the atrophic muscles is as a rule considerably diminished.

*Sensations* are not altered in the area of distribution of the fifth nerve. *Special senses* are not involved.

The gradual but progressive involvement of the medulla leads to *cardiac and pulmonary disorders*. The pulse is small, irregular and feeble; attacks of syncope are quite frequent. The least effort brings on dyspnea. The patient is unable to expectorate, to breathe properly: mucus accumulates in the bronchial tubes. An ordinary bronchitis becomes thus very serious. Bronchopneumonia develops easily. Death occurs from three causes: *inanition* (because of the inability of swallowing), *syncope* and *bronchopneumonia*. The last may be of infectious or gangrenous nature when food enters the larynx. The usual duration of the disease is from a few months to a couple of years.

**Diagnosis.**—The essentially chronic and progressive course after an insidious and slow onset, the successive involvement of the tongue, lips, face, palate and masticatory muscles, atrophy of the muscles with fibrillary contractions and reactions of degeneration are sufficiently characteristic symptoms for the diagnosis of bulbar palsy.

Palsy of the palate following diphtheria is accompanied by difficulty of swallowing and a nasal intonation of the voice. These cases will be recognized by absence of paralysis of the tongue and lips.

In acute bulbar diseases similar localized paralyses may occur, but they are sudden in onset and very frequently accompanied by symptoms referable to the motor and sensory tracts.

In pseudo-bulbar palsy there is always a history of one or two attacks of apoplexy. The syndrome of labioglossolaryngeal paralysis is usually established after the second attack, but it has not the chronic character of the true bulbar palsy. Besides, there is no muscular atrophy

or fibrillary twitching. The spasmodic laughing and crying, impairment of intelligence, hemiplegic condition of the extremities, are all typical of pseudo-bulbar palsy.

*Asthenic bulbar paralysis* (mysasthenia gravis) is recognized by the predominance of the paralysis in the muscles of mastication and in the levator palpebrae (ptosis). The extreme exhaustion manifested in the muscles upon the least exertion, the absence of atrophy and special electrical reactions are characteristic of myasthenia gravis.

**Treatment.**—Counter-irritants to the neck, galvanism of the nuchal and atrophied muscles, belladonna or atropin for the salivation, antiluetic remedies, artificial feeding because of difficulty of swallowing—are all the therapeutic means at our command. Tracheotomy is recommended in cases of threatening asphyxia.

### E. PSEUDO-BULBAR PALSY

**Pathogenesis and Pathology.**—The muscles of the tongue, face, lips, larynx and pharynx are supplied by a lower or peripheral system of neurons which connect the muscles with the nuclei of the medulla, and by an upper system of neurons which connect the bulbar nuclei with the cortex (operculum) and which are situated in the geniculate bundle of the internal capsule. When the first group of neurons is involved, the result will be true bulbar palsy described above. When the second group of neurons (corticobulbar) is affected, there will be an interference with the transmission of stimulation from the brain to the nuclei, and we will have a pseudo-bulbar palsy. If in the latter case the lesion is unilateral, the complete picture of bulbar paralysis will be absent, because the muscles of the pharynx, larynx, the masticatory muscles, those of the forehead and eyelids, receive bilateral cortical innervation. For this reason in cerebral hemiplegia, for example, bulbar symptoms are absent. In pseudo-bulbar palsy, therefore, the lesion must be bilateral.

The seat of the lesion may occur bilaterally in the third frontal convolution (Brissaud), in the basal ganglia, in the cortex of one hemisphere and in the basal ganglia of the other. It may occur in bilateral involvement of the motor segment of the internal capsule. In some cases pseudo-bulbar palsy occurred in unilateral disease of the brain, but the lesion was found to be very severe, such as extensive hemorrhages which, through the mechanism of pressure, produced also disturbances in the other hemisphere. As to the nature of the lesion, it may be hemorrhage, softening, islets of sclerosis (in disseminated sclerosis), cysts. Any condition which is apt to produce a morbid state of the cerebral blood-vessels will cause the lesions mentioned. Syphilis, with its changes in blood-vessels and with gummatous focal disturbances, arteriosclerosis, and cardiac diseases are, therefore, the chief factors.

Oppenheim called attention to a cerebrobulbar paralysis. It occurs when atheromatosis of arteries is not confined to the cerebrum but invades also the medulla, so that changes (softening, etc.) appear

either successively or simultaneously in the cerebrum and in the nuclei of the cranial nerves within the medulla.

Infantile pseudo-bulbar paralysis has been observed in connection with diplegia. It is congenital and due to an arrested development or malformation of the lower parts of the central convolutions.

**Symptomatology.**—In the majority of cases there is a history of several successive apoplectic attacks. After the first attack, hemiplegia will appear with some slight disturbance of phonation, speech and deglutition, the latter usually disappearing soon. It is only after a second apoplectiform seizure that a complete picture of bulbar palsy is established. All the symptoms of a true labioglossolaryngeal paralysis will be observed here, namely: immobility of the facies, stupid expression of the latter, a continuously open mouth, dribbling of saliva, paralysis of muscles of the cheek, lips, tongue, palate, and of those of mastication, of the vocal cords, abolition of the pharyngeal reflex; finally a nasal intonation of the voice, dysarthria with or without aphonia, dysphagia, difficulty of respiration with attacks of dyspnea. (*See* section on Bulbar Palsy.) The posture of the body is rigid, the head bent forward, the movements are spastic.

Contrary to what is observed in bulbar paralysis, the pseudo-bulbar variety can be distinguished by the absence of atrophy and of fibrillary tremor, by preservation of normal electrical reactions and reflexes in the muscles innervated by the bulbar nerves. To this may be added a unilateral or bilateral hemiplegia, frequent involvement of the optic nerves (neuritis or atrophy), finally mental symptoms. The latter consist of a marked impairment of memory, of apathy, confusion and dementia.

A very characteristic phenomenon of pseudo-bulbar paralysis is the facility with which the apparently rigid and immobile musculature can be set in motion under the influence of slight stimulation (emotional or somatic). Moreover, the response to the stimulation is also accomplished in an increased manner. The reason lies in the interruption of inhibition, which is normally transmitted to the bulbar nuclei through the corticobulbar fibers. Thus the masseter reflex is exaggerated and upon stroking the lower half of the face, contractions appear in the orbicularis oris resembling sucking movements (Toulouse and Vurpas). Stimulation of the palate produces contractions of cheeks and upper lip (Henneberg). Stimulation of the lips causes rhythmic movements of the lips, tongue and the lower jaw (Oppenheim). Insignificant provocations produce spasmodic attacks of crying or laughing, which are accompanied by distortion of the muscles of the face and by exaggerated movements of respiration. The eyeballs, ordinarily immovable, follow auditory or optic stimulations in every direction.

In pseudo-bulbar paralysis motor disturbances in the extremities are always present. They are due to the bilateral cerebral lesions, or, as mentioned above, to a unilateral but extensive lesion. Exceptionally, in the so-called senile abasia of Naunyn the lesion is limited to the cerebral centers and the pseudo-bulbar paralysis will manifest very slight motor disturbances in the extremities.

In some cases there may be an extension of the original cerebral lesion to other portions or centers. Thus may be observed: aphasia, hemianopsia, auditory disturbances, disorder in equilibrium, disturbances of deep and superficial sensations, choreo-athetotic movements. Finally, disturbances of the sphincters of the bladder and rectum are frequently present from the beginning of pseudo-bulbar paralysis.

**Course and Prognosis.**—The disease is essentially progressive, but slow in its course. It may be interrupted or aggravated by recurrent apoplectic seizures. The outlook is serious, as the termination is almost invariably fatal. However, with proper attention to the increased reflex activity of the bulbar centers (*see above*), immediate danger from disturbances of deglutition can be avoided. The disease may last many years.

**Diagnosis.**—The sharply defined positive and negative symptoms will enable one to differentiate this form from the true (chronic) bulbar palsy. The acute bulbar palsy will be recognized by the presence of true bulbar focal symptoms and the crossed hemiplegia or hemianesthesia. Amyotrophic lateral sclerosis with bulbar symptoms will be recognized by the localized muscular atrophies, by the absence of mental symptoms and by the course of the disease without apoplectic attacks.

**Treatment.**—Antiluetic medication may be tried in every case, even without a clear specific history.

## F. ASTHENIC BULBAR PARALYSIS

(*Myasthenia Gravis or Pseudo-paralytica of Erb and Goldflam*)

**Pathology and Pathogenesis.**—Various changes in the brain and spinal cord have been reported by some authors and denied by others. In many cases the autopsy findings have been absolutely negative and for this reason the disease has received the name of *bulbar palsy sine materia*. However, some findings deserve to be mentioned. Degenerative changes in the thymus (Weigert,<sup>\*</sup> Hansemann, Goldflam), tumors in the thymus and mediastinum, also in the lungs, degenerative changes in the thyroid, parathyroid, and pituitary body were found in some cases. Ependymitis of the aqueduct of Sylvius has been reported. The muscles are very frequently altered: infiltration of the cells between the fibers and hyaline degeneration are present. Pel found leukocytosis in the parenchymatous organs. Knoblauch found a preponderance of light muscular fibers. Buzzard<sup>119</sup> gave the name "lymphorrhagia" to the infiltrated groups of lymphocytes scattered between the cells of the nuclei in the medulla and he considers them characteristic of *myasthenia gravis*.

Several theories have been advanced to explain the *pathogenesis* of the disease. One of them is the multiglandular view. According to this, the altered internal secretions of various glands play an important rôle in the myasthenic syndrome. (Changes in the glands have been found in a number of cases.) Massolongo<sup>120</sup> believes that whatever the rôle of the gland with internal secretions may be, the presence of a special

inherent predisposition of an organic or morphological character of the bulbospinal centers is necessary. There is, he believes, an inherent weakness of the gray motor centers of the mesencephalon and of the spinal cord which produces muscular exhaustion following any exertion. Oppenheim calls attention to the fact that in many myasthenics there is a congenital hypoplasia of the nervous system and of other organs.

Myasthenia gravis developed in a number of cases after infectious diseases and intoxications, facts which plead in favor of a toxic origin of the disease. Trauma and overexertion have been recorded as exciting causes. Women are more frequently affected than men. The age is between 20 and 40, and in children the disease occurs rarely.

**Symptoms.**—Very gradually, and after a brief prodromal period consisting of headache, occipital pain and vertigo, paralytic phenomena of the muscles of the eye make their appearance. Ptosis is the first symptom. The patient is compelled to contract the frontal muscles to assist the levator palpebræ in raising the eyelids. Very soon appears external ophthalmoplegia, so that strabismus and diplopia are among the earliest manifestations. Later on the seventh and sixth nerves become involved. At the same time, difficulty of phonation and deglutition makes its appearance. The muscles of the neck become gradually involved, so that the patient cannot hold up his head, which has a tendency to fall forward or backward. This is quite characteristic of the disease. When the facial nerve is involved, both portions of it (upper and lower) are paralyzed. This fact, together with the ptosis, gives the facies a peculiar aspect: the face is immobile, without wrinkles, and the impression is one of somnolence. In a more advanced stage, the muscles of the trunk, of the abdomen and of the extremities show signs of weakness and fatigue. The patient is unable to sit up or stand up and has difficulty in breathing; dyspnea is marked on the least exertion. In the shoulder muscles the weakness is very marked—the patient is unable to hold up his arms.

In spite of the paralysis or paresis of the muscles of a more or less long duration, muscular atrophy is extremely rare, fibrillary contractions and reactions of degeneration are entirely absent. On the other hand, one finds a special muscular response to electrical stimulation. This is the so-called "*myasthenic reaction*." It is an exhaustion reaction and consists of a gradual diminution and finally of a loss of contraction when a faradic current is applied to the muscles. If after a brief rest the current is reapplied, the same phenomenon will be observed. This reaction is not obtained from galvanism.

Sensations, reflexes and the function of the sphincters remain intact. The reflexes become exhausted after frequent tests. Mentality is also preserved. The sensory cranial nerves (optic, olfactory, auditory, glossopharyngeal and others) are always intact. The disorder is limited in well-developed cases to the muscles of the eyes (third, fourth and sixth), also to those of mastication (masseter and temporal) and of swallowing (soft palate, pharynx and esophagus). One of the most characteristic features which distinguish this affection from other bulbar

diseases, is the remarkable variability in the paralytic phenomena. Thus, for example, at a certain time of the day, especially in the morning, the muscles perform their functions well, but, after a certain amount of activity, they get more and more exhausted. The patient may begin to speak, but gradually the voice gets weaker and finally complete aphonia sets in. He may attempt to whistle or blow out a candle; at first the acts are normal, but a second and third attempt is almost impossible. Briefly speaking, the disease is characterized by symptoms of paresis or paralysis occurring through increased fatigue.

**Course and Prognosis.**—The disease develops gradually and in the majority of cases has a descending course commencing with the muscles of the eyes; but there are also observations showing that it may begin in the extremities and ascend. Occasionally it may assume an acute form.

When the disease has reached its climax, the patient becomes permanently bedridden. Nutrition suffers from the deglutition paralysis. Death may ensue through respiratory and cardiac paralysis, or be brought about slowly by aspiration pneumonia. Death may also occur suddenly.

Remissions are not infrequent and in light cases recovery is possible (Erb, Goldflam, Steinert).

**Diagnosis.**—The characteristic phenomena of the onset, gradual descending development of symptoms, the facies, myasthenic reactions, and especially the influence of fatigue on the paretic condition of the muscles—these are sufficient for a correct diagnosis. From the chronic form of bulbar paralysis, the acute will be distinguished by the absence of atrophy, of fibrillary contractions and of reactions of degeneration.

**Treatment.**—Absolute rest is indispensable in view of extreme exhaustion upon the slightest effort. Special care should be taken of the **act of deglutition**; slow eating is to be urged. Artificial feeding must be resorted to as soon as difficulty arises, but the **stomach-tube** is to be used with the greatest caution, as death has been observed during its passage.

The presence of the myasthenic reaction in the affected muscles is a direct warning that **electricity is a dangerous procedure**. In view of the tendency of the muscles to become easily fatigued, **gymnastic exercises** are contra-indicated.

**Adrenalin, extract of thymus and thyroidin** have given some favorable results in a certain number of cases (Raymond, Buzzard). Sizary suggests<sup>121</sup> that, when adrenalin is given in adequate doses, benefit will be derived. He has seen cases in which subcutaneous injections of the whole extract or ingestion of fresh adrenals succeeded when the powder and epinephrin had failed completely. His experience demonstrates that certain slow changes in the adrenals, alone or with changes in other ductless glands, may induce a myasthenic syndrome. This justifies organotherapy supplementing the adrenal with hypophysis treatment.

Among other remedies, **iodids, arsenic, phosphorus, iron and strychnin** may be tried.

#### G. HEMORRHAGE AND SOFTENING OF THE MEDULLA

The same causes that produce cerebral hemorrhage and softening are at work here. Traumatism, infectious disease, intoxications, eclampsia are the causes of hemorrhage. Syphilis is a frequent cause of thrombosis and cardiac diseases of embolism.

**Symptoms.**—The clinical picture is that of labioglossolaryngeal paralysis. The difference lies in the rapidity of development of the symptoms. In hemorrhage, the sudden onset may be followed by immediate death, or, after a comatose period (of days or hours), consciousness may be regained and then symptoms of bulbar paralysis will be in evidence (*see* page 478). In softening, the bulbar symptoms will develop gradually after a prodromal period of headache, somnolence and vertigo.

If the patients survive (which will occur rather in softening than in hemorrhage, in which death is the usual termination), there will be present the same symptoms as in typical chronic bulbar paralysis, except that their distribution is not as symmetrical as in the latter.

A special type of thrombotic softening in the medulla was described first by Hahn<sup>122</sup> in 1897 under the name of "*occlusion of the postero-inferior cerebellar artery.*" Spiller has recently presented this subject in all its details. The clinical picture is as follows: sudden onset with or without loss of consciousness, unilateral paralysis of the palate and vocal cords; difficulty of swallowing and expectorating, hemiataxia, syringomyelic sensory dissociation on the opposite side. In the author's case<sup>123</sup> there was right hemiasynergia; tendency to fall to the right side; pain in the neck; paresthesia on the left side where the objective sensory dissociation was present; paresis of the right side of the face; retraction of the right eyeball; narrowing of the right pupil.

**Pathologically** the disease is characterized by a softening in one half of the medulla. The area affected lies between the spot where the artery begins to pass to the cerebellum and the middle of the nucleus of the hypoglossus. The formatio reticularis with its nuclei, the descending root of the fifth nerve, the nuclei of the seventh and ninth nerves, also the spinocerebellar tract, are all involved.

#### H. COMPRESSION OF THE MEDULLA

The medulla may be compressed (*a*) *suddenly*, by dislocation or fracture of the atlas or axis; (*b*) *slowly* by tumors in the medulla itself or in the neighboring tissue and organs, by caries or other diseases of the neighboring bony tissue, by basal meningitis and, quite frequently, by aneurysms of the basilar or vertebral arteries. In the sudden cases, the tissue of the medulla may be destroyed. In the slow cases, the



medulla will be deformed or softened. Secondary degeneration is the consequence.

**Symptoms.**—In case of gradual compression, pain in the occiput and neck is the first symptom. The head is kept by the patient in absolute immobility. Active and passive movements provoke pain. When the compression extends downward to the cervical cord, pain will be present also in the upper extremities. In cases of aneurysm of the basilar or vertebral arteries, in addition to occipital pain, there will be also vertigo, tinnitus aurium and other symptoms of arteriosclerosis. Bulbar compression will be manifested by disturbances of deglutition, of respiration, of heart beats, but what is especially characteristic is the intermittent bulbar manifestations (dysarthria, dysphagia, dyspnea, arrhythmia, tachycardia). After the latter have existed for a certain time, they gradually improve and then disappear until the next attack. Through injury of the motor and sensory tracts, there will be corresponding symptoms (hemiplegia, paraplegia). Sensory disturbances of the syringomyelic type are not rare. A myosis on the side of the lesion will be present if it (tumor) interrupts the tracts which lead to the sympathetic nucleus of origin in the dorsal portion of the spinal cord.

A very important symptom was pointed out by Hallyoupeau, Giraudeau and Killian: the heads of the patients are held in forced extension; as soon as they are flexed, respiratory disturbances occur.

When the compression is produced by a tumor, in addition to the above special symptoms, there will be also general symptoms of intracranial neoplasms.

**Course and Prognosis.**—In sudden compression, death is sudden from respiratory paralysis. In slow compression, the patient is constantly threatened with rupture of aneurysm or softening or destruction of the tissue of the medulla. Cardiac and respiratory disturbances are usually fatal. The outlook is grave, although the disease may last months or years.

**Diagnosis.**—The diagnosis is based in the slow cases on the gradual development of the symptoms and on the pain in the neck, also on the flexion phenomenon of the head.

**Treatment.**—The treatment is only administration of **antisiphilitic remedies**.

## I. TUMORS OF THE FOURTH VENTRICLE

What was said of the affections of the lateral and third ventricles is largely applicable here. Tumors of the fourth ventricle produce symptoms of hydrocephalus or those of pressure on the neighboring tissue, viz., cerebellum, pons and medulla. According to the seat of predominant pressure, corresponding predominant symptoms will be present, either from the cerebellum, or pons, or medulla. Thus there are cases in the literature which presented the picture of cerebellar tumor, others of the bulbar symptom-group, etc.

In all cases, apart from general symptoms characteristic of increased intracranial pressure, there are also a characteristic stiffness of the neck

and pain in the occipital region. In view of the fact that in fourth ventricle tumors there is an increase of pressure of the spinal fluid, also an increase in cells and globulin in the latter, the disease was not infrequently taken for meningitis.

The seriousness and gravity of tumors localized in the fourth ventricle should not be overlooked in considering operative procedures. On the other hand, Anton<sup>124</sup> calls attention to the fact that in some cases the tumors were found to originate in the choroid plexuses and are not, therefore, attached to the walls of the ventricle. He also observed that some tumors were found attached to the vermis of the cerebellum. He, therefore, argues that it is not at all impossible to enter the ventricle through the vermis, explore it and, if the tumor is not adherent to the wall, to remove it. Anton always advises a preliminary puncture of the corpus callosum or of the lateral ventricles in order to relieve at first the intense intracranial pressure.

#### LOCALIZING DIAGNOSIS OF BULBAR SYMPTOMS

A. When the lesion lies at the level of the olivary bodies (anterior bulbar syndrome of Dejerine), there will be crossed hemiplegia: the twelfth nerve or its nucleus will be involved on the side of the lesion, but the arm and leg will be paralyzed on the opposite side, because the decussation is below the lesion.

B. When the lesion is in the lower portion of the medulla (retro-olivary bulbar syndrome of Dejerine), there will be paralysis of the soft palate and larynx, also of certain muscles of the head and neck associated or not with a contralateral hemiplegia. Here we meet with several varieties, according to the extension of the lesion in height and width. They are as follows:

(1) *Schmidt's Syndrome*.—Unilateral paralysis of the soft palate, of the vocal cord, of the sternomastoid and trapezius muscles. We have here a total paralysis of the eleventh nerve.

(2) *Jackson's Syndrome*.—Unilateral paralysis of the soft palate, of the vocal cord, of the sternomastoid and trapezius muscles, also of the tongue which undergoes atrophy. We have here total paralysis of the eleventh and twelfth nerves. In some cases the picture may not be complete and the unilateral paralysis affects only the tongue and the soft palate.

(3) *Tapia's Syndrome*.—Unilateral paralysis of the tongue and vocal cord. It is, therefore, a glossolaryngeal paralysis and the lesion is in the twelfth and tenth nerves below the plexiform ganglion. It is of peripheral character.

(4) *Avellis' Syndrome*.—Unilateral paralysis of the soft palate and the vocal cord, also a contralateral hemianesthesia of syringomyelic type. The former is due to the involvement of the internal branch of the eleventh nerve with the vagospinal nucleus, the latter to the involvement of the crossed sensory fibers of the formatio reticularis. In the largest majority of cases, all four varieties are accompanied by

motor or sensory disturbances or both on the opposite side. The sensory disturbances may be of pure syringomyelic type or may be in the domain of all forms of sensations—deep and superficial. The paralyzed muscles are atrophied.

With the exception of Avellis' syndrome, in all the other three the lesion is more frequently in the peripheral nerves than in their roots or nuclei.

(5) *Babinski-Nageotte's Syndrome*.—Myosis, enophthalmia and slight ptosis on the side of the lesion, hemiplegia and hemianesthesia on the opposite side with hemiasynergia and tendency to fall toward the side of the lesion.

#### XIV. CEREBELLUM

The cerebellum contains two important portions which are physiologically independent of each other: cortex and central gray matter. The cerebellar hemispheres are in connection with the cortex of the brain and basal ganglia. The vermis is in connection with the pons, medulla and spinal cord.

The function of the cerebellum has been the subject of many investigations. Beginning with Flourens (1827), we find a large array of highly authoritative physiologists, to mention only a few, Wagner, Lussana, Luciani, Ferrier, Turner, Munk, Lewandowsky, Bechterew, Horsley, Clark, and finally André-Thomas, all of whom endeavored to solve experimentally various problems concerning the function of the cerebellum. The last author particularly has made attempts to conciliate the findings from experimentation with those of clinical observation, corroborating both by anatomical proofs and thus explaining the mechanism of the manifestations observed in man and animal. Although all these investigations threw considerable light on the subject, nevertheless some of its phases are still obscure and the problem of the function of the cerebellum is far from being definitely solved. Speaking generally, it is established that the functions of the cerebellum are *not in the psychic sphere* and that the cerebellum is especially concerned in *motility*. Here we encounter several opinions: Luciani believes it to be an organ of energy for muscular tonus; Lussana and Lewandowsky consider it in connection with muscular sense; Munk and especially André-Thomas think that it is essentially an organ of equilibrium. Maintenance of equilibrium and regulation of all movements are the essential functional characteristics of the cerebellum. Although the sensorimotor zone of the cerebral cortex and the labyrinth participate in the maintenance of equilibrium, so that, in case the cerebellum is removed, motion and equilibrium are not entirely abolished, nevertheless the cerebellum plays a very important rôle in this function. In view of this observation, the question naturally arises whether the cerebellum has an independent influence on muscle movements and whether its different lobules bear a special relationship to the different muscle groups, as Bolk<sup>125</sup> among the first had advocated, or whether the func-

tion of the cerebellum is only to exert its influence on the motor cortex of the brain and the paracerebellar nuclei in the medulla, thus regulating their activities.

Besides Bolk, experimenters such as Adamkiewicz, Van Rynberk, Rothmann and others arrived at the following conclusions: The vermis possesses centers for the muscles of the head and neck, trunk, and each



FIG. 13.—TUMOR OF THE VERMIS.

hemisphere has centers for the muscles of the homolateral limbs. Each center of the upper and lower limb has secondary centers for each segment of the limb and for each individual movement upward, downward, internally and externally. André-Thomas and Durupt<sup>126</sup> have shown that each of these centers is dynamogenic for a group of muscles, but inhibitory for the antagonistic muscles. A lesion of each of these centers causes a disturbance in the equilibrium of the antagonistic muscles—a defect which explains the various phenomena of the cerebellar syndrome discussed below.

The view of cerebellar localization is combated by Luciani, and others, who believes that the cerebellum is a homogeneous structure and when one portion of it is deficient, the remaining portion quickly compensates it. The view of the cerebellum possessing the function of regulating the cerebral cortex is shared by Mills and especially by Myers. The last author in a recent contribution<sup>127</sup> presented the subject in a highly suggestive manner. Basing his arguments on personal experimentation, he holds that the function of the cerebellum is to inhibit, control and regulate the activity of the motor cortex of the cerebrum and the paracerebral nuclei in the medulla; that the cerebellum is functionally differentiated for the various muscle-groups of the body, *indirectly*, by being primarily related through its various lobules to the various motor centers in the cerebrum and the tonus center in the medulla, just as the posterior root ganglion is, in a motor sense, related to a certain muscle-complex through its corresponding group of motor cells in the anterior horn of the cord.

Which of these views is the correct one it is difficult to say in the light of our present knowledge. What is certain is the fact that the disturbances observed in various diseased conditions of the cerebellum are fundamentally of a *motor* order.

#### CEREBELLAR SYNDROME

(a) **Station.**—The legs are separated. The body oscillates so that sometimes the patient is obliged to hold on to some object. The instability is particularly marked in change of position. In order to keep his equilibrium, the patient often spreads out his arms.

(b) **Gait.**—The patient is unable to walk along a straight line. His oscillations increase. In mild cases he resembles a person who is afraid of losing balance. In pronounced cases he resembles an inebriate person who walks from side to side (*titubation* or zigzag-like) (*cerebellar ataxia*). Standing or walking with the eyes closed does not increase the disturbance of equilibrium. The Romberg sign is, therefore, absent. Standing on the leg corresponding to the lesion is less steady than standing on the sound side. In walking there is a tendency to go toward one side and the head and trunk are also inclined to the same side (side of the lesion).

(c) **Cerebellar Asynergy.**—Under the name of *cerebellar asynergy*, Babinski, in 1899, described a disturbance of associated movement. It is elicited in the following acts: (1) In walking, the movements of the lower limbs and of the trunk are dissociated, the trunk does not follow the legs in their forward movements; (2) in an attempt to throw the head back and curve the trunk in the same direction, the legs remain immovable or almost immovable, contrary to what is observed in normal condition when the legs and thigh flex; (3) when, lying on his back, the patient attempts to sit up, he raises his legs and flexes them on the pelvis; (4) when, seated on a chair, the patient wishes to rise on his leg, he first flexes the thigh on the pelvis and then only c

evate the leg. The latter movement is produced very abruptly; in order to put the foot back upon the ground, the leg first flexes over the thigh, then abruptly the latter becomes extended and the foot reaches the floor.

The disturbed associated movements just described may be confined to one side and they are then spoken of as *hemiasynergy*.

(d) **Dysmetria**.—Babinski called attention to the difficulty of regulating movements. The latter are executed without measuring the time and space: either they are too rapid and abrupt, so that the object is overstepped (*hypermetria*) or else they are executed slowly and do not



FIG. 14.—CEREBELLAR ASYNERGY.

Attitude of walking; patient held by two assistants. (After Babinski.)

reach the object (*hypometria*). The tests are as follows: When the patient attempts to walk, he will raise his feet higher than normally, which means excessive flexion of the thigh over the pelvis. When he wishes to put his finger on the nose, the former will overstep the point of destination and reach the cheek; but when at last it reaches the nose, the hand is unstable and performs several movements before it is settled. André-Thomas and Jumentié recommend the following two tests: (1) *Grasping*: in grasping a glass the patient opens his hand more than it is necessary; the same is observed in releasing the glass. (2) *Pronation and supination*: when with arms extended forward and thumbs upward the patient pronates his hands, the act is exaggerated and the thumb goes down lower on the affected side than on the sound side; the same exaggeration of movement is observed in supinating the hand.

Dysmetria may be also observed in movements of the lower extremities: When in dorsal position the patient is told to touch the opposite knee with the heel, the latter is raised too high and oversteps the point of destination. The same phenomenon is seen when the patient attempts to touch any object with his foot.

Dysmetria is an important factor in the phenomenon of *Adiadokokinesia* (Babinski). It consists of difficulty or inability to execute rapidly consecutive pronation and supination of the hand; care must be taken to ascertain that there is no paralysis of the hand. The same difficulty is experienced by cerebellar patients in alternating flexion and extension of the forearm, in opening and closing the hand, in flexing and extending the fingers. *Adiadokokinesia* is due to a slowness of each individual movement. A *delay* in execution of voluntary movements is characteristic of cerebellar cases. It is more marked in acts executed to order than in spontaneous acts.

Dysmetria, which is due to defect in association of synergic movements, is the chief cause of the disturbed equilibrium in station, in gait, in execution of any movement, in the above-mentioned *asynergia*. Dysmetria is especially evident in *rapid* movements. When the patient executes acts slowly, the movements are more or less correct. Therein lies the reason why movements in cerebellar patients appear to be slow.

André-Thomas called attention to a phenomenon of discontinuity of movement, or "*intentional tremor*." It consists of interruptions in execution of an act: The patient does the act in sections; there is, otherwise speaking, no continuity in movement. The trembling phenomenon is observed especially in the beginning of the act or in the effort of maintaining a certain given attitude.

The dysmetria has its influence on writing: the latter is generally altered, the letters are irregular and unequal. For the same reason, very probably, the speech is in some cases dragging or else explosive, the syllables are accentuated as in multiple sclerosis.

(c) **Resistance.**—Holmes and Steward, and especially André-Thomas, called attention to abnormal, voluntary and passive movements in cerebellar cases. According to the first two writers, in a unilateral involvement of the cerebellum, while the patient is flexing his arm on the affected side and the examiner opposes this flexion with his hand and then suddenly removes the latter, the movement of the flexion continues and the hand strikes the chest violently (which shows a delay in the movement of the antagonistic muscles). In normal conditions, the arm will continue, for a moment, flexing at first, but will immediately stop and move in the opposite direction. In passive movements André-Thomas<sup>128</sup> observed that when the arm is raised to a horizontal position and the forearm given repeated abrupt movements, the arm on the side of the cerebellar lesion shows very little resistance, the movements of flexion followed by movements of return (extension) are both of greater amplitude than on the normal side where resistance is greater and the movements are slower. Similarly, when both elbows are held and alternately adducted and abducted, the resistance is less

marked on the affected than on the sound side. In the lower extremities, if the thighs are placed at a right angle to the pelvis and the legs extended, but immediately abandoned, the leg on the affected side shows less resistance and its return to the hanging position is more rapid than that of its fellow on the sound side. The same is observed in the movements of abduction and adduction. When the thighs are flexed on the pelvis and the legs on the thighs, and alternate movements of abduction and adduction are carried out, less resistance is observed in the leg of the affected than in that on the sound side. This, according to Thomas, is more marked in the abductors than in the adductors. He also observed that when the patient is in dorsal position and the leg on the side of the lesion is in outward rotation and then placed in inward position, the foot promptly turns outward. On the other hand, when the foot is forcibly rotated externally and abandoned, it returns to its former position less rapidly and less completely than the opposite leg.

(f) **Spring-like Phenomenon** (André-Thomas).—It is seen in the following test: When the patient is told to raise his arm (of the affected side) and to let it fall on his head, it will do so like an inert body, namely, it will rebound several times. The same may be observed in the finger-to-nose movement.

(g) **Catalepsy** (Babinski).—It consists of a special ability to maintain a fixed position longer than normal. When a patient, lying on his back with his thighs flexed over the pelvis and the legs over the thighs, raises his limbs, the latter at first will oscillate from side to side, but in a few moments the trunk and limbs will become fixed. This fixation may remain for several minutes and is not followed by fatigue.

(h) **Hypotonia and Asthenia**.—Luciani called attention to these phenomena on the side of the lesion as characteristic of cerebellar diseases and especially of tumors. Muscular weakness may be observed in both cerebral and cerebellar conditions. It is especially evident in the test for dysmetria. When the latter is of cerebellar origin, it follows usually abrupt or rapid movements. In cases of hemiparesis of cerebral nature, certain movements are exaggerated. Thus, in grasping or releasing an object, the fingers place themselves in hyperextension and abduction, but what is characteristic is the marked slowness and decided weakness of the movement.

(i) The *position of the head* deserves special mention. In 1908 the author<sup>129</sup> called attention to a head phenomenon which he found of localizing value in a series of cases, some of which came to autopsy. It consists of increase of vertigo or headache or of both when the head is turned to the side of the seat of the cerebellar lesion (especially tumor). *Stiffness of the neck* is quite common; it is probably due to pressure upon the dura in the posterior fossa. *Fixed position* of the head, mostly toward the side of the lesion (tumor), with great resistance to any passive change, is frequently observed.

(j) **Rotatory Vertigo** (Holmes and Stewart).—It consists of a subjective sensation of objects moving from the side of the tumor to the sound side.



(*k*) **Nystagmus.**—Nystagmus is almost a constant symptom. It is more marked in lateral than in vertical movements of the eyes. It is usually slow and of wide range toward the side of the lesion, but of smaller range and more rapid toward the normal side.

(*l*) **Tendon Reflexes.**—They are usually altered. All varieties may be present, from diminution and loss to exaggeration. A unilateral change does not always correspond to the seat of the lesion. André Thomas calls attention to the following characteristics of the tendon reflexes. When the patient is placed on an elevated seat with his legs hanging down, without touching the floor, and the usual test is made for the patellar tendon reflex, the normal knee-jerk will consist of a sudden extension of the leg and slow return to the position of rest. On the diseased side, if the reflex is present, the movement of extension is of a somewhat greater amplitude and is followed by a series of flexion and extension movements. This reflex is called by Thomas "*the pendulous type*." The same form of reflex is observed in the biceps and triceps for the upper extremity in unilateral cerebellar lesions. These abnormal reflex phenomena, as well as the abnormal passive and voluntary movements, are all indicative of a disorder in the display of the antagonistic muscles and, if present, are localized together with other unilateral cerebral symptoms on the side of the lesion. They are all pathognomonic.

#### CEREBELLAR HEMIPLEGIA

This term was introduced by Pierre Marie and Foix, who used it first in studying cerebellar hemisyndromes with a *sudden onset* and caused by arterial lesions of luetic origin.

**Pathology and Symptoms of Various Forms.**—The term "hemiplegia" does not here imply a unilateral paralysis at all, but the occurrence of cerebellar symptoms, such as ataxia, asynergia, etc., on one side and suddenly. In a recent thesis, J. Thiers,<sup>130</sup> basing his arguments on observations of other writers and his own, considers two main forms of cerebellar hemiplegia: (1) of central origin and (2) of tract origin.

(1) *Cerebellar Hemiplegia of Central Origin.*—It occurs either suddenly, following a hemorrhage or softening, or develops gradually as a result of an intracerebellar tumor (tubercle, gumma, abscess, glioma) or an extracerebellar growth, such as cerebellopontine.

(2) *Cerebellar hemiplegia of tract origin* is secondary to an involvement of the cerebellar peduncles. It is met with in old cases of syphilis and caused by vascular changes of a degenerative or inflammatory process. The onset is sudden, accompanied by vertigo without loss of consciousness. If the lesion remains confined to its original seat, there are no sensory changes, the cutaneous reflexes are normal, the toe phenomenon is absent, and the knee-jerks are but very slightly increased. In some cases the lesion may invade the neighboring tissues; the pyramidal tract is then involved and, according to its involvement

above or below the commissure of Wernicke, the symptoms will be homolateral or crossed.

Thiers considers three varieties, according to the peduncle affected:

(1) In the *superior* variety, in which the cerebellopyramidal syndrome is homolateral, there may be an association of thalamic syndrome (cerebellothalamic form), or there may be palsy of the sixth nerve on one side and cerebellar hemiplegia on the other (cerebello-ocular form); or else there may be the cerebellopyramidal symptom-group with dysarthria.

(2) In the *middle* variety, which is due to a lesion of lateral pontine artery, there are crossed cerebellopyramidal symptoms with or without sensory disturbances.

(3) In the *inferior* variety (bulbar) there are: hemiasynergy, lateropulsion, myosis and hemianesthesia with hemiplegia.

**Course.**—The chief forms of cerebellar hemiplegia differ in course: Contrary to what is seen in the central form, the symptoms of the *tract form* persist indefinitely after a slight improvement. The **prognosis** must be made guardedly in view of the underlying syphilitic arteritis.

In making a **differential diagnosis** with cerebral hemiplegia, one must bear in mind that in cases with an apoplectic onset, after consciousness is regained, there is no true paralysis in cerebellar hemiplegia, that there is no contracture, no spasticity, no toe phenomenon, no ankle-clonus, that the homolateral weakness affects all the muscles of the involved limbs, while in cerebral hemiplegia only certain muscular groups are affected, such as flexors of the leg and foot, extensors of the hand. If paralysis develops in cerebellar hemiplegia, it is almost never at the beginning, but later, and it is due to pressure upon the pons and medulla.

#### CEREBELLAR PARASYNDROME

This was described by André Léri<sup>131</sup> as observed on a wounded soldier. The bullet entered immediately below the external occipital protuberance and injured the superficial part of the inferior vermis. Simultaneously, all the elements of the cerebellar syndrome made their appearance, viz., Duchenne's group (titubation, tremor, vertigo) and Babinski's group of symptoms (asynergia, adiadokokinesia, catalepsy), but all these symptoms remained confined to the *lower extremities*. It is, therefore, evident that in the inferior vermis there is a center for coordination of the lower extremities, a lesion of which (center) will produce the cerebellar parasyndrome. A detailed analysis of this observation leads to the following conclusions on the pathogenesis of the cerebellar syndrome:

(1) *Titubation* is independent of atony or asthenia. It is equally independent of vertigo, because titubation appears only in gait or standing, while vertigo is present during active or passive inclination of the head anteroposteriorly. (2) *Asynergy, adiadokokinesia* and *tremor* may occur without the least trace of dysmetria, contrary to the opinion of some writers who attributed the first to the existence of the latter.

(3) *Vertigo* of cerebellar origin may be the consequence of the displacement of the head in one (sagittal) direction; it seems that there is a distinct relation between the cerebellar cortex and the semicircular canals. (4) *Opisthotonos* may be the result of a lesion of the inferior vermis in man as well as in animals.



FIG. 15.—TUMOR OF THE PONTOCEREBELLAR ANGLE.

The *cerebellar syndrome* described on the preceding pages may be encountered in all varieties of cerebellar lesions. However, in unilateral *hemorrhage* and *softening* the homolateral symptoms are frequently temporary and compensation is rapidly established. Superficial or cortical softening of the cerebellum often passes unnoticed. It is in *tumor* and *primary atrophy* of the cerebellum that the cerebellar syndrome is observed in all its entirety. In 1900, Dejerine and André-Thomé described such a case under the name of *Oligo-ponto-cerebellar Atrophy*.

## CEREBELLAR TUMORS

**Pathology and Symptoms.**—In some cases they are confined to the cerebellum: they originate in the hemispheres or in the vermis and may remain there during their entire course of development; they may, however, overstep the limits of the cerebellum, and, in becoming enlarged, will press upon and displace neighboring tissue. Other tumors, originating in the vicinity of the cerebellum, compress the latter or its peduncles, also the centers and nerves connected with it. As an example may be mentioned tumors of the pontocerebellar angle (*see* page 470). Lesions or tumors originate in the meninges or in the cranial nerves; they may be localized on the cerebellar pathways or on their centers of origin, viz., the three cerebellar peduncles and the cerebellar tracts of the spinal cord (Gowers' and direct cerebellar tract). Consequently, lesions of the mesencephalon, pons and medulla may present symptoms of the cerebellar syndrome. It is in tumors that disturbances of equilibrium reach their maximum. The reason for this probably lies in several factors, viz., hypertension of the cerebrospinal fluid, direct pressure at the seat of origin of the tumor and pressure at a distance, finally the disturbance caused by the tumor in the vestibular apparatus which is intimately connected with the cerebellum and cerebellar tracts. As is well known, the internal dorsal nucleus, Deiters' and Bechterew's nuclei, in which end the fibers of the vestibular roots, are in relation with the central nuclei of the cerebellum, especially with the nucleus of the roof and the globulus, by means of the internal semicircular fibers which enter the dentate nucleus and go through the superior cerebellar peduncle. The nucleus of the roof is in close relation with the vermis, and the dentate nucleus with the cortex of the hemispheres of the cerebellum.

Tumors of the *vermis* present very marked disturbances of equilibrium in station and gait. There is a tendency to fall either forward or backward; nystagmus is constant. II. Jackson observed also convulsive seizures.

In addition to the cerebellar syndrome and the general symptoms characteristic of all intracranial neoplasms, such as headache (which is frequently occipital), vomiting and vertigo, which occur quite early, there are *special eye symptoms* and *neighborhood symptoms* in cerebellar tumors.

(a) *Eye Symptoms.*—The eye-grounds show hyperemia, edema, choked disk, optic atrophy. The pupils are frequently unequal. Nystagmus with its special characteristics was already described in the preceding pages. *Skew deviation* of the eyes is sometimes observed: it consists of one eye looking downward and inward, the other outward and upward.

(b) *The neighborhood symptoms* are: When the tumor is on one side the trigeminal nerve may be involved; there will be at first *areflexia* of the cornea (Oppenheim) and later sensory disturbance over the area of distribution of the involved fifth nerve. The sixth, seventh and

twelfth nerves may become paralyzed and, from pressure on the brain stem, there will be either a hemiparesis, or hemiplegia, or else a crossed paralysis. The hemiplegia is not spastic, the face is not involved and hypotonia of the muscles is present on the affected side. The toe phenomenon and ankle-clonus may be absent.

When the tumor is located anteriorly in the cerebellum, it may affect the quadrigeminal bodies and the occipital lobes, and thus present phenomena characteristic of those parts of the cerebrum (*see* pages 440 and 426).

**Diagnosis.**—In a certain number of cases the diagnosis of a cerebellar tumor presents some difficulty. In the initial stages, when only general symptoms are present, the localizing diagnosis is embarrassing, for the symptoms are common to cerebral growths. When, however, in addition to the general symptoms, bulbar manifestations make their appearance, the presumption is in favor of a cerebellar involvement. As to the seat of the tumor, one must look for unilateral symptoms. Particular stress must be laid upon hemiasynergy, adiadokokinesia, dysmetria, position of the head, nystagmus, state of reflexes on one and the other side, involvement of cranial nerves, unilateral occipital headache, with tenderness on percussion of the occiput, etc. (*see* Cerebellar Syndrome).

Cerebellar ataxia must not be confounded with tabetic ataxia. The zigzag movements (titubation), the resemblance of this gait to that of an inebriate person, are not present in tabes. The raising of the feet high and dropping them with force upon the ground are characteristic only of the tabetic. For past-pointing symptoms see section on Cerebellar Abscess. Since Cruveilhier, in 1829, there have appeared occasionally in the literature cases with cerebral lesions simulating cerebellar involvement. In one group of these cases there were cerebral lesions with crossed cerebellar atrophy (Monakow, Mott, Launois, Mingazzini, Lhermitte, Kononova and others). In another group of cases there were direct foci in the cerebrum, but no material lesions in the cerebellum and the symptoms were those referable to the latter. Bruns<sup>12</sup> reports 4 cases of frontal tumors giving during life cerebellar symptoms. In Bernhardt's book on "Hirngeschwülste"<sup>13</sup> there are references to 40 per cent. of frontal tumors with ataxia resembling that of cerebellar diseases and in 12 per cent. of cases a similar condition was observed in tumors of other regions than frontal. O. Fragnito<sup>14</sup> has recently reported a case of tumor in the right frontal lobe which developed as a clinical picture of the cerebellar syndrome. In the contribution alluded to in the section on Frontal Lobe, the author presented four anatomicoclinical cases, all with lesions in the frontal lobe (sarcoma, abscess, cyst, hemorrhage), but without involvement of the cerebral region. In all four cases a cerebellar diagnosis was justifiable, in view of the presence of many elements of the cerebellar syndrome. But in analyzing the cerebellar phenomena in the four cases, it was found that the symptoms were not all localized on one side, that they were irregularly distributed over both sides of the body, although they were re-

lar in character. There was a distinct *dissociation* of the symptoms and to a degree that, if a cerebellar involvement were entertained, its definite localization would have been difficult, if not impossible.

Individually considered, some of the characteristic cerebellar symptoms may be encountered in lesions (tumors) of the frontal lobe. In Hitzig's<sup>132</sup> case, for example, the resemblance of the ataxia to one of cerebellar origin was such that the diagnosis of cerebellar tumor was made, the patient was operated in the occipital region, but in reality the tumor was situated in the frontal lobe. If, however, one or several symptoms may present difficulty in differentiation as to whether they are of cerebral or cerebellar origin, the presence or absence of other phenomena, such as those of André-Thomas, or of Holmes and Steward, will render valuable aid in establishing a diagnosis of localization. But, above all, the most important differential sign is found in "the dissociation of localizing symptoms." The *non-coexistence* of cerebellar symptoms *on the same side* speaks against a cerebellar lesion.

As to the anatomicophysiological reasons of similarity between diseases of the frontal lobe and of the cerebellum, Mingazzini's anatomical data, corroborated by Flechsig, von Monakow and others, are sufficiently evident. According to him, frontocerebellar pathways run through the anterior segment of the internal capsule, descend and, after forming one-fifth of the foot of the cerebral peduncle, surround the pyramidal groups of fibers, cross at the level of the posterior extremity of the pons and enter the middle cerebellar peduncle on the opposite side. It is, therefore, logical to admit that a lesion of the cerebrum suppressing its activity will at the same time interfere with the function of the fibers emanating from the lesion and will thereby carry its morbid influence to the subjacent nuclei and through them to the cerebellar hemisphere. Thus are explained the various cerebellar manifestations in cases of frontal lobe lesions.

**Course, Duration and Prognosis.**—The general symptoms may persist for several months before titubation and other characteristic phenomena make their appearance. The duration of the disease is indefinite. It may last from several months to several years, although in the majority of cases it runs a rapid course. The termination is fatal in cases which are not operated upon, although a few cases of recovery of tuberculoma of the cerebellum have been reported. Rapid termination occurs in cases of compression of the medulla. Of all varieties of tumors, tuberculoma is the most frequent. Tubercle of the cerebellum is rarely solitary and never primary; it is almost always accompanied by pulmonary lesions.

**Treatment.**—Relief and removal of distressing symptoms may follow the administration of **antiluetic remedies** even in cases of tuberculous tumors. Operative procedures are to be considered eventually in every case. **Decompression** early performed may prevent blindness, besides giving relief from intolerable headache. The suboccipital route is the proper method.

## ABSCESS OF THE CEREBELLUM

The most frequent cause is suppuration of the temporal bone, which is a common occurrence in chronic otitis media. Occasionally it may follow an acute otitis media. The otitis itself may develop in the course of influenza, pharyngitis or some infectious disease. Staphylococci, streptococci or pneumococci are usually found in the pus of the abscess, which is thick, greenish and fetid. The nervous tissue undergoes softening and destruction. The meninges are diseased; phlebitis of the sinuses and thrombosis are frequent.

**Symptoms.**—**GENERAL.**—Headache is constant and persistent. Vomiting is not frequent, but its disappearance and recurrence at intervals are quite characteristic. Insomnia is very persistent. Somnolence and vertigo are constant, the latter occurring upon the least movement of the head. The mentality as a rule is not disturbed. Rigidity of the neck and retraction of the head are frequently met with. Optic neuritis and papillitis with edema (choked disk) with considerable loss of vision are common. The temperature oscillates between one or two points above or below normal. Bradycardia is common.

**SPECIAL SYMPTOMS.**—(1) *Cerebellar Syndrome (Unilateral).*—This consists of: ataxia, adiadokokinesia, dysmetria, etc. (see this section).

(2) *Nystagmus.*—It is of *vestibular* type, viz., a quick movement in one direction and a slow movement in the opposite direction. It is mostly rotatory; it is constant and persistent, which distinguishes it from nystagmus observed in labyrinthitis; in the latter the nystagmus has a tendency to disappear, and it is always toward the sound side.

(3) *Past-pointing.*—With eyes closed, the patient faces the examiner, stretches out his arm and holds his extended index finger in contact with that of the examiner. He is told to lower the arm and again bring the finger to the former position. It is then observed that the patient's finger will deviate outward from the examiner's finger only with the hand corresponding to the side in which the cerebellar abscess is localized, but there will be no error in pointing with the opposite hand. When the ear on the sound side is irrigated with cold water, the resulting nystagmus will be in the opposite direction. If at that time the same test is performed with the arms, it will be found that, while the left arm moves to the left, the right arm deviates as before to the right. The loss of normal reaction in pointing on spontaneous test and on vestibular irritation are pathognomonic of abscess of right cerebellar hemisphere.

(4) *Neighborhood Symptoms.*—Compression of neighboring portions of the nervous system will produce crossed paralysis, viz., involvement of any of the cranial nerves on one side and of the extremities on the opposite side, which is indicative of pressure at the base of the brain.

**Diagnosis.**—The main lesions which cerebellar abscess may be confounded are: (1) temporosphenoidal abscess, and (2) labyrinthitis. In a *cerebral abscess of the temporosphenoidal region* nystagmus is exceedingly rare; equilibrium may be disturbed, but it is not of the unilat-  
eral character of cerebellar conditions; besides, the asynergia, adia-

kinesia, etc., are absent; hemiparesis (when present) is always contralateral; oculomotor disturbances, hemianopsia, some degree of aphasia and paraphasia are all present; vertigo is not of recurring character; tenderness of the head on the side of the abscess is deep-seated, intense and persistent; mentality is always dull and delayed.

In *labyrinthine diseases* in which the vestibular apparatus is involved, there are signs which are also met with in cerebellar lesions (abscess, tumor, etc.), but there are some which differ from those of the latter. The *common symptoms* are: In standing the patient is obliged to keep his legs wide apart; he cannot stand on one foot; the gait is uncertain, walking is from side to side; the steps are irregular and unequal; muscular energy is diminished and the patient is easily fatigued.

The *differential symptoms* are: In labyrinthitis Romberg's sign is present, but it is absent in cerebellar diseases; change of position of the head increases greatly the disturbed equilibrium in vestibular cases; vestibular ataxia is a static ataxia which does not modify individual movements of the limbs, while the latter are greatly disturbed in cerebellar cases (dysmetria, etc.); in a vestibular case submitted to movements of rotation, the orientation of these movements is no more perceived: nystagmus and rotatory vertigo disappear, caloric proof of Bárány is negative, also the galvanic test produces no vertigo and no nystagmus (*see these tests below*).

**DIAGNOSTIC TESTS.**—In view of the importance of knowledge of the function of the vestibular apparatus in connection with the study of the cerebellum, a description of tests employed in the elucidation of symptoms referable to the former follows:

A. *Romberg's Test*.—It consists of standing with heels and toes together and eyes closed. In vestibular lesions the preservation of equilibrium is impossible. Station on one foot is more difficult on the side corresponding to the lesion than on the other. If, while the eyes are closed, the patient's head is abruptly turned to one or the other side, the patient will show a tendency to fall only toward the affected side in vestibular lesions, but in intracranial lesions always in the same direction, irrespective of the position of the head.

B. *Stein's Test*.—Ewald and Goltz have shown that pigeons deprived of their semicircular canals cannot adapt themselves to surroundings by proper muscular movements, if they are moved from place to place. André-Thomas observed the same phenomenon in dogs whose auditory nerves had been cut. When such an animal is placed on a platform which is being moved laterally, anteriorly or posteriorly, it will fall in the corresponding direction. Stein's goniometer consists of a movable platform so arranged that it can be inclined at various angles. The tendency to fall as seen in the animals will reveal a lesion of the vestibular apparatus. This test is not frequently employed, as it requires a special apparatus and because other tests give excellent results.

C. *Nystagmus Test*.—Stimulation of the vestibular apparatus in normal persons is followed by nystagmus, but when the apparatus is



diseased nystagmus is not produced. The mode of stimulation may be *mechanical, caloric and electric*.

(1) *Mechanical*.—Nystagmus is the result of contractions of the motor muscles of the eyes due to a stimulation of the semicircular canals; the direction of the movement is determined by the direction of the endolymph movement of the given canal. The nystagmus is horizontal when the horizontal canal is stimulated, and rotatory when the horizontal and vertical canals are stimulated. In testing the horizontal semicircular canal, the patient is seated on a revolving chair, the eyes closed, the head resting and tilted thirty degrees forward (Jones). The chair is turned about one dozen times and suddenly stopped. The eyeballs are immediately examined and a nystagmus is observed. When the turning is done to the right, it has reference to the left labyrinth and *vice versa*. Nystagmus is pronounced in normal conditions, but it is absent or markedly diminished in pathological conditions of the vestibular apparatus.

For testing the vertical semicircular canals, the patient is placed on a turning table in a dorsal or lateral position, and the examination is made as before.

(2) *Caloric* (Bárány).—It is done either with *cold* or *warm* water:

(a) *Cold Water*.—Water of a temperature about 70° F. is allowed to run in a continuous stream for about 40 seconds into the auditory canal. Nystagmus then appears: It is in the direction opposite to the injected ear when at the same time the eyes are turned there; it is usually rotatory in character and only sometimes horizontal; it lasts one or two minutes.

(b) *Warm Water*.—The temperature must be only slightly above normal. The irrigation lasts 60 seconds. The nystagmus is rotatory, as in the cold water test, with this difference: that it is in the opposite direction, viz., it is in the direction of the irrigated ear if the eyes are also turned there. It lasts 2 or 3 minutes.

The caloric test influences only those canals which are in a vertical plane. The nystagmus changes the direction and its form from rotatory to horizontal when the head is inclined toward the right or left shoulder, anteriorly or posteriorly.

When the caloric test is positive, the semicircular canals are intact; in vestibular diseases the test is negative. The caloric test has this great advantage, that it enables one to examine each ear separately, contrary to the mechanical test, which stimulates both labyrinths simultaneously.

(3) *Electric* (Babinski).—Two electrodes of a galvanic current are placed in front of both tragus. In normal conditions, with a current of 2.5 milliamperes, the following symptoms are observed: While the patient is standing, there will be inclination of the head and trunk, turning of the eyes and nystagmus toward the positive pole, and at the same time there is vertigo. In labyrinthine diseases, all these phenomena will be absent with a current of the same strength (2.5 milliamperes), but they will make their appearance with a much stronger current, viz., of 10-12 milliamperes, and then the falling will be toward the

affected ear, irrespective of the direction of the current. However, Babinski in his later researches found that "the inclination of head" as well as "the vertigo" present great variations and that the variability itself is an indication of disturbances either in the posterior labyrinth or in the vestibular nerve.

*Spontaneous Nystagmus.*—Spontaneous nystagmus may be sometimes observed in *labyrinthine affections*. In such cases Bárány observed the following disturbances of equilibrium: When the patient is placed in Romberg's position, he shows a tendency to fall in the plane of the nystagmus but in the direction opposite to that of the rapid movement of the nystagmus. When the head is turned to the right, the patient falls forward; if turned to the left, he falls backwards. On the contrary, in *cerebellar diseases* Bárány observed that there is no relation between spontaneous nystagmus (which is frequently present) and the direction of falling; neither has the position of the head any influence upon the direction of the falling. On the other hand, the manifestations will be identical in both cerebellar and labyrinthine affections in induced nystagmus.

D. *Past-pointing after Turning.*—The patient is placed on a revolving platform in the same position as in the test for nystagmus (see above). After the tenth turn, the patient is no more able to place his forefinger on the object before him and he makes mistakes: if the turning of the platform is done, for example, from left to right the finger will past-point to the right of the object. In diseases of the cerebellum, without a preliminary vestibular stimulation (such as turning), a persistent past-pointing in one or other direction is of a diagnostic value.

#### CEREBELLAR HEREDO-ATAXIA

Under this name Pierre Marie described a form of cerebellar incoordination hereditary in character and occurring in several members of the same family. Pathologically it was characterized essentially by atrophy or sclerosis of the cerebellum. Autopsy records of these and other cases show that the cerebellum is rarely alone affected, that in some cases, in addition to the above, there was also sclerosis of Goll's, Gowers' and the direct cerebellar tracts, also atrophy of the middle cerebellar peduncles (in Marie's first case), atrophy of the entire cerebrosplinal axis (Minra's case), meningeal lesions in Frazier's case.

*Symptoms.*—Station and gait are similar to those of cerebellar ataxia. The lower extremities are affected long before the upper. The gait is slow and uncertain, the legs are separated: the patient gives the impression of being about to lose his equilibrium at any moment. The body oscillates while walking; titubation is constant. The entire "cerebellar syndrome" (see above) is present. The reflexes are increased. As the disease progresses, the upper extremities become involved: their movements become uncertain; a fine intention tremor is frequently present, so that delicate acts, such as writing, threading a needle, etc., are almost impossible. The speech is irregular; each word

is accentuated and precipitated; the voice is monotonous and guttural. When the patient speaks, there is noticeable an exaggerated contraction of the muscles of the face.

The psychic faculties are usually altered. Impairment of intelligence, of memory, irritability and indifference are the main disturbances observed.

The evolution of the symptoms is gradual. Neurasthenic symptoms precede the disturbance of equilibrium, but the disease is invariably progressive, although it may remain stationary for some time. In its last period there is absolute physical impotence: the patient is confined to bed and usually dies from some intercurrent disease. The age at which the disease makes its first appearance is between 15 and 25 years.

**Diagnosis.**—In making a diagnosis there will be no special difficulty in *differentiating* the disease from tumors, hemorrhages or abscesses of the cerebellum, but there will be some difficulty in distinguishing it from Friedreich's ataxia. In favor of heredo-cerebellar ataxia will be the family character, the age at which it occurs, the slow development, cerebellar gait and other elements of the cerebellar syndrome, the peculiar facial mimicry, intention tremor, finally increased knee-jerks with ankle-clonus. The condition of the knee-jerks is particularly important, as their loss is characteristic of Friedreich's ataxia. The latter affection may present sometimes, especially at the beginning, normal reflexes, and in Marie's disease, when the lesion reaches the cord, the reflexes may be abolished. In all such cases, the other symptoms will aid in making a diagnosis.

In 1903 Batten<sup>133</sup> described a symptom-group which he called "*congenital cerebellar ataxia*." The chief symptoms are: onset in early life, unsteadiness of head, trunk, and limbs, unsteadiness in sitting, in standing, in walking, slowness in swallowing, alteration in articulation, finally, a tendency to recovery. In all of Batten's cases the characteristic speech, a mild degree of ataxia and a mildly uncertain gait remained.

In 1913 Clark<sup>134</sup> called attention to a series of cases exhibiting cerebellar ataxia accompanied by mental defect. In his cases the most characteristic feature was an unusual flaccidity of the limbs, especially in the upper extremities. There were also ataxia in all four extremities, straddling gait, dysmetria, but no changes in the reflexes. There was, as in Batten's cases, a tendency toward improvement, especially in the cerebellar manifestations, viz., in the ataxia, station, gait and hypotonia, but the speech and mental defect remained unaltered.

In 1916,<sup>135</sup> and later in 1917<sup>136</sup> and 1918,<sup>137</sup> the author presented under the title of "*Cerebrocerebellar Ataxia*" a series of records of cases which resemble, in the majority of their manifestations, those of Batten and Clark, but differ in some respects: While in the cases of Batten and Clark the patellar, tendon and plantar reflexes were normal, in the author's cases the knee-jerks were markedly increased, ankle-clonus

and toe-phenomenon were present. The improvement was also uniform in the cerebellar manifestations.

While there were present some differences in the clinical pictures of the former two investigators and of the author, such as the state of the reflexes and the state of tonicity of the muscles, nevertheless the essential features are identical in all, namely: (1) the invariable association of cerebral and cerebellar symptoms; (2) the tendency to improvement, especially in the manifestations referable to the cerebellum. The difference lies only in the predominance of one group of symptoms over the other. These differences indicate only the existence of varieties, and the type of the disorder deserves a place in the nosology of the central nervous system. It seems logical to assume that Friedreich's disease, Marie's cerebellar heredo-ataxia, Batten's, Clark's, and the author's cerebrocerebellar ataxia belong to a vast group of "abiotrophic" conditions and are probably due to a congenital defect or an agenic abnormality in the cerebrum and cerebellum.

## B. INTRACRANIAL HYPERTENSION AND TUMORS OF THE BRAIN

### INTRACRANIAL HYPERTENSION

**Pathology.**—Intracranial hypertension is due fundamentally to an increase of pressure of the cerebrospinal fluid. The effect produced by the latter on various cerebral centers is found in a number of diseases of the brain, i.e., tumors, encephalitis, hemorrhages, and especially in various meningeal states.

The cerebrospinal fluid constitutes a sort of a liquid bed in which rest various portions of the brain and spinal cord. It fills the ventricles which communicate with each other through foramina. It reaches the subarachnoid spaces which form a sac for the cord. The sac becomes enlarged at the lower end of the cord. The subarachnoid spaces of the brain are in communication with the ventricles through Luschka's foramina. These spaces are small on the surface of the brain, but they are particularly developed at the base of the brain, where they present actual reservoirs; they are all in communication with each other. They are crossed by the cranial nerves which are thus bathed in the fluid.

The cerebrospinal fluid is chiefly secreted by the choroid plexuses of the ventricles. (The reader is referred for elaboration of this subject to the section on Hydrocephalus.) The amount of fluid secreted is from 80 to 150 c.c. The fluid is in communication with the spaces surrounding the blood-vessels entering the brain. It penetrates also the space around the nerves, especially those of the olfactory, optic and the spinal roots, after which it follows the lymphatics of the peripheral nerves. Thus the mechanism of transmission of infectious processes is

explained. In the perivascular spaces, as shown by Mott, and in the perineural spaces, the cerebrospinal fluid is absorbed.

It is quite well established that the cerebrospinal fluid possesses a circulation. Its secretion, also pressure in the ventricles and subarachnoid spaces, are all regulated by the circulation of the blood.

Its pressure is inferior to that of the arteries, but higher than the venous pressure. This difference facilitates its absorption. It is, therefore, evident that in certain conditions disturbances in arterial or venous pressure may influence the pressure of the cerebrospinal fluid.

Other causes besides the vascular factor may create modifications in the pressure of the cerebrospinal fluid, i.e., disturbances in the circulation within the ventricular cavities and subarachnoid spaces, also inflammatory conditions and mechanical irritation. Disturbances in the venous circulation, especially in compression of Galen's veins, will produce edema in the choroid plexuses, hence an increase of secretion. An inflammatory state of the ventricular cavities due to infectious processes, such as occurs in meningitis, will lead to the same results. Here a mechanical obstacle must be taken into consideration with regard to the permeability of the ventricles and subarachnoid spaces, obstacle created by the inflammatory process.

Obliteration of the aqueduct of Sylvius, caused by occlusion of Luschka's foramina or by edema of the neighboring parts, will interfere with the free communication between the ventricular and subarachnoid cavities, with the result that the ventricles will be dilated.

Various degrees of hypertension and ventricular dilatation will be observed, according to the degree of obstruction in the communicating foramina, to the amount of the intraventricular secretion conditioned by the inflammatory state, finally to the degree of permeability of the subarachnoid space, especially at the base of the brain. (*Consult section on Hydrocephalus.*)

The diseases in which the above pathogenic conditions of hypertension may be realized are as follows: First of all, tumors of brain, particularly those of its central portions, i.e., thalamus, epiphysis, temporo-occipital region, cerebellum and hypophysis. Less commonly it is observed in tumors of the cortex or pons. Next in order of frequency are the encephalopathies of children which are usually accompanied by infectious ependymitis. Here the ependyma and choroid plexuses are in a state of inflammation. In adults, the encephalopathies have for cause syphilis, tuberculosis and toxo-infectious processes.

Meningitis, acute or tuberculous, especially in children, is frequently accompanied by hypertension. Occasionally this may be observed in the course of cerebral hemorrhage or softening. Finally, it may be observed in various infectious diseases and inflammatory processes of the cranial cavities, i.e., sinusitis, mastoiditis, otitis and ocular affections.

**Symptoms of Hypertension.**—Four important manifestations constitute the chief characteristics of the hypertension syndrome.

**A. HEADACHE.**—It is the earliest symptom. It may appear gradually or suddenly. Sometimes it is preceded for weeks by a sensation of

heaviness in the head. The headache is unusually severe, the patient feels as if the head is going to split open. He is so overwhelmed by the pain that he becomes dull and unresponsive to stimulation; there is mental hebetude. While the headache is continuous, nevertheless there are also paroxysms of exacerbations, especially on motion. During the paroxysms, the patient's behavior gives the impression of approaching syncope: the face is very pale and covered with cold perspiration, there is a tendency to vomiting, the pulse is feeble and rapid. After the paroxysm is over, the headache is somewhat lessened.

The headache is, as a rule, diffuse, but is sometimes localized. Sometimes percussion of the cranium will reveal a very tender area which not infrequently corresponds to the seat of tumor, but this is not absolute in every case of tumor. The headache cannot be relieved by ordinary means, but yields to lumbar puncture or decompression.

B. VOMITING.—Vomiting is a frequent accompaniment of the headache. It may follow or precede the latter. Frequently it is abundant and takes place especially on motion. Nausea may or may not precede it. Its pathogenesis is probably of labyrinthine origin, in view of the fact that hypertension may easily influence the vestibular apparatus.

C. VISUAL DISTURBANCES.—They constitute the most important symptom. An ophthalmoscopic examination must be done in every case in which there is persistent headache with vomiting. The papilla is at first red, the veins are dilated and tortuous, edema soon makes its appearance. In some cases there is stasis without edema. In cases with stasis the pupils are dilated and do not respond to light. The patient is totally or almost totally blind. The papilla shows a venous congestion; the veins are dilated, and more tortuous than in edema; there may be also hemorrhages. The visual acuity is *nil* or almost *nil*. Gradually, if there is no improvement, the stasis leads to atrophy. The papilla is then white, the arteries are small, the veins may remain dilated for a long time.

As to the pathogenesis of papillo-edema, the latter is attributed to the effect of hypertension upon the sheath of the optic nerve, thus producing disturbances in the vascular and lymph circulation of the latter. This view is particularly upheld by Hippel.<sup>138</sup> It is also held by C. H. Frazier, who, from personal surgical experiences, observed that, when intracranial pressure was increased to a considerable extent, there was papillo-edema, but when, in the presence of a tumor, large or small, tension was not increased, there were no changes in the eye-grounds. Cushing, Bordley and Heuer have recently shown that alterations of the color fields (inversion) frequently occur in intracranial tumors as an early manifestation. The following peculiarities were noticed by them: (1) A tumor may advance slowly and be accompanied by cerebral edema or other pressure symptoms; distortion of the color fields (dyschromatopsia) may be the earliest indication of the latter and observed on the side opposite to the lesion. (2) Unilateral dyschromatopsia, accompanied by an incipient degree of choked disk, may be on the same side of the lesion and is, therefore, of localizing value; if dys-

chromatopsia is bilateral, the higher degree of it is on the side of the lesion. (3) Dyschromatopsia is a more delicate manifestation of intracranial pressure than papillo-edema.

D. ALTERATIONS OF CEREBROSPINAL FLUID.—Increased pressure of the cerebrospinal fluid can be ascertained during lumbar puncture, when it escapes as a strong flow, and by means of a manometer. However, there is no absolute relation between the hypertension of the fluid, as stated, at lumbar puncture and the intracranial hypertension. In tumors, for example, in spite of all the clinical evidences of hypertension, the writer observed that lumbar puncture brought forth the spinal fluid drop by drop. When the stream of the escaping spinal fluid is strong, one is justified in the conclusion of high pressure, but the reverse is not against increased intracranial pressure. The reason of the latter may be found in obliteration of communications between the spinal, arachnoid and ventricular cavities. In chronic meningitis, there are adhesions which interfere with the circulation of the cerebrospinal fluid, so that the hypertension may remain localized in the brain. The permeability of the subarachnoid spaces may be only diminished, and lumbar puncture, by abruptly lowering the tension in the spinal arachnoid spaces, produces modifications in the pressure of cerebellar spaces and ventricles, thus leading to changes in the relations of various portions of the cerebrum. The procedure is, therefore, not without danger, especially when one deals with cerebellar tumors which have a tendency to compress the medulla. The variations and the permeability of the communicating orifices explain different effects obtained from lumbar puncture and other ways of decompression.

More decisive and important diagnostic information concerning hypertension can be determined from chemical, biological and cytological examinations.

*Chemical.*—Almost always the content of the *albumin* is increased. Sicard has shown that this increase is particularly pathognomonic when it is not accompanied by cytological changes (albumino-cytological dissociation). According to the same author, hyperalbuminosis is present when it is found in quantity of 0.60 per 1000 of spinal fluid. Quincke believes that, if the quantity of albumin is above 2 per 1000, we deal with serous meningitis. According to K. Werzel, in hydrocephalus the albumin content is 1 to 2 per 1000.

The presence of *fibrin* in the cerebrospinal fluid is important for diagnosis of cerebral neoplasms. Spontaneously or after addition of fresh serum it coagulates. Almost always fibrinosis is accompanied by a yellowish taint of the fluid.

*Cytological examination* shows that in a large number of cases there is no increase of *lymphocytes*, or else the increase is slight and cannot serve for diagnosis of cerebral neoplasms. If lymphocytosis is present, it may be syphilitic only if the Wassermann reaction is positive.

The foregoing remarks concerning the cerebrospinal fluid tend to show that neither albuminosis alone, nor the cytological state by itself, nor an increased tension as obtained on lumbar puncture, is sufficiently

constant for one to form a definite and precise idea concerning intracranial hypertension. It is only a combined examination for all its various properties that will enable one to arrive at diagnostic conclusions regarding the cerebrospinal fluid.

The *headache, vertigo* and *visual disturbances* are, generally speaking, the fundamental features of intracranial hypertension. They may be present without other symptoms, but in the majority of the cases they are associated with other manifestations.

*Vertigo* may be accompanied by disturbances of the vestibular nerve. There may be epileptic phenomena of local or generalized character, motor phenomena as demonstrated by increased defense, and tendon reflexes and toe-phenomenon, or else by absence of reflexes. There may be sensory manifestations, such as lancinating pain, or paresthesia, or radicular anesthetics due to pressure on the spinal roots. There may be hypo-acusia, tinnitus aurium, parausic phenomena, disturbance of memory, mental hebetude, somnolence, indifference, tendency to syncope, slowness of pulse, finally cranial palsies, especially of the sixth and seventh pairs of nerves. In some cases, the syndrome of intracranial hypertension will be complete, in others incomplete. Sometimes it will give the picture of bulbar or cerebellar cases, or else of labyrinthine cases.

In a small group of cases there will be no or almost no headache, but there will be vomiting; pyloric stenosis will be then suspected or the diagnosis of neurasthenia will be made.

It is, therefore, evident that, if in some cases the diagnosis of intracranial pressure forces itself, there are cases in which the abnormality of the symptoms or their absence is likely to mislead and remove all thought of the disorder. One must always bear in mind this possibility if vertigo, amaurosis or amblyopia, hemiplegia, etc., are present. The examination of the papilla must be made repeatedly and systematically.

**Causes of Intracranial Hypertension.**—*Hydrocephalus* and *cerebral tumors* are the chief factors. (The effect of tumors is largely due to a hydrocephalic condition.)

*Acute and chronic meningitis* (tuberculous, syphilitic, etc.) are accompanied by hypertension. In young children, when the cranial bones become separated in the course of chronic meningitis, the relation of the latter to hydrocephalus is evident. In adults, chronic syphilitic meningitis, especially of the base, may present the symptoms of a tumor, but a biological examination will soon permit a differentiation. The four reactions of Nonne, i.e., positive Wassermann of the blood and of the spinal fluid, albuminosis and lymphocytosis, will clear up the difficulty.

Certain meningeal states in Bright's disease may give the impression of tumor of the brain. There may be vomiting and visual disturbances. There is uremic hypertension. But in uremia the papilla is different from that in cerebral neoplasms, viz., there is only edema; hemorrhages are more abundant, and there are white brilliant spots,



probably deposits of cholesterin. Besides, the urinalysis will reveal the usual characteristics of nephritis.

When in presence of hypertension syndrome meningitis or uremia are eliminated, true hydrocephalus or tumor of the brain are to be thought of.

(1) *Congenital hydrocephalus*, with a large head, stasis or edema of the papilla, diplegia, epileptic convulsions and mental disturbances, is frequently of luetic origin. It may also have for cause saturnism or bacterial infection of slow evolution. The pure cases of hydrocephalus are characterized by symptoms of hypertension without localizing signs. It is difficult to differentiate such cases from tumors of the brain, as there are cases of tumor without localizing signs, also there are cases of hydrocephalus with localizing symptoms.

(2) *Tumors of the brain*.

## TUMORS OF THE BRAIN

The influence which a brain tumor exercises is twofold: one influence is local, the other is on the entire brain and its cavities. A tumor of long duration will affect its vicinity and injure it by pressure; there will be, consequently, besides *local* and *general* symptoms, also "*neighborhood symptoms*." Direct pressure produces displacement of the brain toward the point of least resistance (which is usually the ventricles), flattening of the convolutions and destruction of nerve elements. The cerebrospinal fluid is increased, so that the entire brain is wet (edema) and internal hydrocephalus may be produced. The latter condition is particularly marked in tumors situated in the vicinity of the foramina connecting the ventricles, as, for example, near the middle lobe of the cerebellum or the quadrigeminal bodies. The increase in tension of the fluid is the result of increased production or of impaired absorption of the cerebrospinal fluid or of both factors (*see* preceding section and section on Hydrocephalus). A tumor, by increasing intracranial pressure, produces an obstacle to the free cerebral circulation, thus causing an increase of the intracranial venous pressure. The latter, as shown in the discussion of mechanism of hydrocephalus, has a direct effect on the cerebrospinal fluid, thus raising its pressure.

The meninges are tense. The area of softening which is seen around the tumor is due to the destruction of the nervous tissue. The latter is an irritative process, which eventually leads to an inflammation. Bergmann advocates the view that brain pressure has a direct effect on the nervous tissue by producing a capillary anemia.

The above-mentioned increase of cerebrospinal fluid takes place not only in the cranium, but also in the spinal canal; the arachnoid of the latter becomes distended and the posterior nerve-roots are thus overextended. Degenerative changes of these roots and of the posterior columns are not infrequently met with in cerebral tumors.

**Symptoms**—They are *general* and *local*.

**GENERAL SYMPTOMS.**—The *general* symptoms are common to almost all forms of tumor irrespective of their seat and nature. They are those of intracranial hypertension in general (*see* preceding section).

**LOCAL SYMPTOMS.**—They correspond to the facts observed from investigations on brain localizations. To avoid repetition, the reader is referred to the section on Cerebral Localizations, in which each portion of the brain, brain-stem and cerebellum was discussed at great length. Suffice it here to make some additional remarks of a general character. There are two regions in the brain in which tumors can be localized with comparative facility. They are: *the rolandic zone* and *occipital area*. Whether they are cortical or subcortical, *tumors of the rolandic zone* can be revealed the earlier precisely because of the stormy reaction of motor cortical cells expressed in epilepsy (frequently of jacksonian type). In some cases hemiplegia reveals the onset of the disease. It may appear suddenly or else develop gradually, commencing with the lower extremity and ending with the upper. In the latter case, the reflexes may be normal and the usual contracture of classical hemiplegia may be absent. In such cases the diagnosis will be based on the associated symptoms, namely, the frequently accompanying epileptic convulsions, aphasia (which may be transitory), the pronation sign, the sign of exaggerated flexion of the forearm over the arm and other signs pointed out by Babinski (*see* Hemiplegia). They are all indicative of extracerebral neoplasms which are merely producing pressure without destroying the cerebral tissue.

When the tumor lies posterior to the rolandic fissure, the early manifestations are: partial epilepsy, very slight motor disturbances, but pronounced sensory phenomena (*see* Parietal Region in Cerebral Localization).

In *tumors of the occipital zone*, the symptoms are equally evident and present no diagnostic difficulty; but they do not appear as early as the symptoms of the rolandic area. It is only exceptionally that the visual fields suffer at the outset. Homonymous hemianopsia without Wernicke's pupil appears late. According to the direction in which the neoplasm grows, there will be also word-blindness or word-deafness.

In any other cerebral region, except those just mentioned, the localizing diagnosis of tumor will present some difficulty. In the so-called silent regions the difficulty is still greater because the associative symptoms of intracranial hypertension may lead to an erroneous diagnosis.

*Tumor of the frontal lobe* may be suspected when the headache is localized in the same area and when there is unilateral exophthalmos, when mental disturbances and moria are present, and when epileptic convulsions are not followed by persistent motor phenomena. Horsley claims that when the aura in epilepsy is psychic, the tumor is in the frontal lobe; when it is olfactory, the tumor is in the cornu Ammonis; and when it is auditory, the tumor is in the temporal lobe.

In *tumors of the base of the brain*, especially in those of the hypophysis, the characteristic symptoms are especially those of the third, fourth and sixth cranial nerves, also of bitemporal hemianopsia. Besides, there

will be evidences of acromegaly or gigantism, or else of adiposogenital syndrome (Fröhlich).

In *tumors of the pontocerebellar angle* the symptoms are almost entirely those of the acoustic nerve. The patient has had unilateral deafness for a long time, suffers from vertigo, has pain in the face or teeth. Gradually a slight facial palsy, and palsy of the sixth nerve are added on the side of the deafness. Motor and sensory disturbances soon appear on the opposite side (*see* this section).

In *tumors of the pons* the early symptoms are hemiplegia and hemianesthesia of the syringomyelic type. The facial paralysis is complete and the sixth nerve is always involved. Cerebellar and sympathetic phenomena soon make their appearance. The disease has a tendency to become bilateral.

In *tumors of the medulla* the symptoms are the same as those of the pontine tumors with this difference: that instead of the sixth and seventh nerves, we have disturbances in the domain of the ninth, tenth, eleventh and twelfth nerves. Glycosuria and polyuria are sometimes present. More frequently than in tumors of other areas, here the pulse is irregular, rapid and there is a tendency to syncope. Sudden or rapid death is also more frequent.

In *tumors of the fourth ventricle* the diagnosis is difficult. We find here ordinary symptoms of intracranial hypertension to which are added titubation, paralysis of associated movements of the eyes without facial paralysis and sometimes deviation of the head (*see* Fourth Ventricle). In *cerebellar tumors*, besides the classical cerebellar syndrome (ataxia, adiadokokinesia, etc.), there is a persistent pain in the occipital region, deviation of the head and paralysis of the associative movements of the eyes. In some cases, the latter three symptoms together with ataxia may exist without the former for a long time, but their presence renders the diagnosis suspicious of cerebellar tumor.

**Course.**—In the majority of cases death is the final outcome of cerebral tumor. The course is slow, especially in gliomata and sarcomata. In these cases the general symptoms are more conspicuous than the local symptoms. Epileptic convulsions usually precede local symptoms for a very long time. Local signs are particularly marked in tumors of areas richly supplied with projection fibers. Focal epilepsy is an early sign in tumors of the motor area.

The progressive development of the symptoms is irregular. Exacerbations of the general symptoms is quite common, but they disappear and reappear, usually leaving a decided aggravation of the condition. The aggravations may be due to sudden hemorrhages within or around the tumor, or else to sudden increase of intracranial pressure.

The localization and the character of the tumor have an influence on the evolution of the disease. Sarcomata grow rapidly, fibromata and endotheliomata, angiomata and enchondromata grow slowly; cysts may remain stationary. Gummata may recover when the patient is treated. Tuberculomata grow rapidly, but when they become calcified, they remain stationary. Cysticerci and echinococci remain frequently sta-

tionary. In aneurysms which usually run a course like that of tumors, death occurs through rupture, but recovery may also occur through organization of the aneurysm.

Death usually occurs in deep coma and it is due to the failure of the bulbar centers to functionate because of increased intracranial pressure. Sometimes death is sudden, especially in tumors of the posterior fossae, through pressure and sudden paralysis of the respiratory center.

**Nature of Cerebral Tumors.**—GLIOMA.—Of all the growths glioma occurs in the largest number of cases and is the most universal in its incidence. Tooth<sup>139</sup> places it at 49.2 per cent. of all cerebral tumors, and at 58.7 per cent. of growths in the forebrain; in the midbrain it predominates to the extent of 50 per cent.; in the cerebellum and pons, including the extracerebellar growths, there are 38.4 per cent. of gliomata.

Glioma is a soft and very vascular tumor. It is not encapsulated but continuous with the neighboring cerebral tissue. The most frequent seat is the white substance beneath the cortex. Histologically it is essentially composed of neuroglia tissue. When, in addition to the latter, there are also connective tissue elements, the tumor is called gliosarcoma. In rare cases (probably congenital), a hyperplasia of the cortical elements is seen besides abundant neuroglia and vascular tissue; it is then called neuroglioma. Gliomata very frequently undergo cystic degeneration. Glioma is seen more frequently in middle life than in old age.

SARCOMA.—No part of the brain can be exempt from sarcoma. It is a soft tumor, but distinctly harder than glioma. It presents this characteristic feature that there is a sharply defined line of demarcation between it and the brain tissue and it is, therefore, separable from the latter. It is frequently encapsulated. It is reddish and of spherical form. In the majority of cases, sarcomata originate in the dura mater, periosteum and bone. They develop frequently at the base of the brain.

There is a variety of sarcoma, characterized by a proliferation of connective tissue, called *fibrosarcoma*. Its multiplicity and localization all over the central and peripheral nervous system, particularly in the cerebellopontine angle, also in the roots of the spinal cord and cauda equina, are the characteristic features of these tumors. Sarcoma occurs particularly in middle life. A very malignant form is the *melanotic sarcoma*, which is a secondary tumor.

ENDOTHELIOMA.—It usually originates in the flat cells which line the inner surface of the dura, but it may also develop from the endothelium of the blood-vessels. When, in addition to the cells, there develops also a large amount of connective tissue fibers, also when it contains calcareous concretions, the tumor is called *psammoma*. Endothelioma occurs at any age.

TUBERCULOUS TUMOR.—Unlike glioma, it has a tendency to become encapsulated. It is the size of a cherry. Its usual seat is in the most vascular areas, i.e., in the fissure of Sylvius, at the base of the brain, in the vicinity of the pons and in the interpeduncular space. The

most common seat is around the pachionian bodies. It is found more frequently near the meninges than within the cerebral tissue. The cerebellum is the favorite seat of tubercles in children. There is frequently more than one tumor. The granular tissue of which the tubercle is composed is formed at the expense of the perivascular sheaths and neuroglia tissue. The tubercle bacillus is frequently found. Tubercular tumors may produce tuberculous meningitis.

**GUMMA.**—It is frequently found in adults. Small in size, irregular and nodular in shape, firm in some parts and soft in others, it is most frequently located at the base of the brain and quite often also in the cortex, especially in the anterior portions of the hemispheres. At the base they invariably involve the cranial nerves or the large blood-vessels, the obliteration of which leads to softening of cerebral tissue. There are often several gummata. Very small gummata are sometimes found around the blood-vessels, so that the resemblance to miliary tubercles is striking, but the latter are extremely small. Gumma is not vascular and on section it presents irregular cheesy spots between which fibrous tissue is seen.

**VASCULAR TUMORS.**—Angiomata are rare, but aneurysms are not very rare. They are usually found on the bends or curves which the arteries form in their course. Statistics show that the basilar artery is the most frequently affected and the next in frequency is the middle cerebral. While the generally adopted view is that syphilis is probably the cause of cerebral aneurysms, nevertheless, Turnbull,<sup>140</sup> basing himself on the findings of the postmortem records in the London Hospital during seven years, proves that the above view needs revision. According to him, only 6.25 per cent. of the aneurysms were due to the inflammatory reaction set up by the activity of *Spirocheta pallida*.

**CYSTS.**—Besides cystic formations developed in place of old hemorrhagic foci or areas of softening (see Apoplexy); there are also some which develop in connection with sarcomata or gliomata. When any of these tumors break down and the débris is carried off, a cavity surrounded by walls composed of the elements of the growth takes its place and thus a cyst is formed. These formations usually occupy the ventricular cavities and are also found in the cerebellum.

Occasionally cysts contain parasites, viz., *cysticercus* and *echinococcus*. The cysticercus is found in the meninges and particularly in the area of the perforated spaces. The latter fact is the reason of the ocular phenomena observed during life. Especially at the base, the vesicle of the cysticercus has a tendency to advance into the fissures. This growth of the vesicle may lead to an inflammatory state of the membranes and to formation of fibrous masses (basal cysticercus meningitis). The echinococcus forms adhesions with the meninges, produces a thinning of cranial bones and may be eliminated through the natural openings of the cranium. It is observed especially in certain countries, Australia, for example. Parvy and Laubry<sup>141</sup> have observed that if the blood serum of individuals having the echinococcus in any other organ contain specific antibodies, the latter are absent in the cere-

bro-spinal fluid, but they will be present if the central nervous system is affected. Recently, Legry, Parvy and Baumgartner<sup>142</sup> reported new proofs of the above observation. A positive deviation of complement in the cerebrospinal fluid and negative in the serum is pathognomonic of a parasitic cyst in the brain when a tumor is suspected and when no other cause could be accounted for.

**CARCINOMA.**—In the majority of cases it is secondary to carcinoma of other organs of the body. It is comparatively frequent in the ventricular cavities or in the walls of the ventricles. It is vascular and rarely encapsulated. It is usually multiple. It occurs mostly in aged people. According to Silvan's statistics, based on 14,000 necropsies, it represents 17 per cent. of all intracranial tumors, the left hemisphere being involved, especially the cortex of the frontal and parietal lobes.<sup>142</sup>

**CHOLEASTOMA AND OSTEOMA.**—These are very rare. The former is easily recognizable by its brilliant appearance.

**Diagnosis of Tumor.**—The general as well as the various local symptoms, in accordance with the seat and nature of the neoplasm, have been largely dwelt upon in the preceding sections, but particularly in the section on Cerebral localizations. In the latter, each cerebral area was discussed *seriatim* and the clinical manifestations presented at great length. The reader is referred to those sections for diagnostic considerations. In the following few lines the salient diagnostic elements will be reviewed and emphasized and some additional features presented.

In tumors as well as in cases of brain pressure in general, beside the characteristic headache, the most valuable information is furnished by the *examination of the eyes*, and of their fundi especially. In the largest number of cases the latter is of decisive importance. Choked disk, viz., the prominence of the head of the optic nerve, occurs more frequently in increased brain pressure than in any other condition. Congestion of the retinal veins may occur also in other affections, such as encephalitis, anemia, chlorosis, multiple sclerosis, as well as in intracranial hypertension. The diagnosis will be then based on the symptoms characteristic of each of these affections, but in difficult cases lumbar puncture must be resorted to. Should the latter prove absence of high pressure of the spinal fluid, affections other than tumor are to be thought of. However, in all such cases one must always bear in mind the occasional discrepancy between an actually existing high cerebral pressure and a slow flow of the spinal fluid during a lumbar puncture (*consult* section on causes of intracranial hypertension).

Another difficulty in the diagnosis of tumor is presented in early cases with very *slight local symptoms*. A very careful and repeated examination will almost invariably reveal some, though extremely mild, indication of functional disturbance on the part of the motor pathway, such as the toe-phenomenon either by Babinski's method, or by the author's procedure (paradoxical reflex), or by Marie's crossed adductor reflex, etc. (*see* Hemiplegia). They may not all be present at the same time, but the existence of even one of them is of diagnostic value.

Recently, Yanishefsky<sup>143</sup> introduced a new phenomenon observed by him in brain tumors, viz., "the grasping reflex." The fingers curl promptly around a stick brought in contact with them when otherwise the patient may have been unable to flex the fingers. One patient with a tumor of the right frontal lobe and left paresis was unable to bend his fingers or open the hand voluntarily, but if a stick touched the volar side of the hand, the object was grasped. According to Yanishefsky, the sign is particularly frequent in tumors of the frontal lobe. Robinson and Preyer noticed this reflex in children up to the age of 84 days.

The occurrence of *jacksonian convulsions, unilateral involvement of the cranial nerves* are especially valuable signs to awaken suspicion of and to localize a tumor.

*Serous meningitis, or acquired hydrocephalus*, may sometimes simulate a tumor (see Hydrocephalus or preceding sections). A lumbar puncture in such cases will render valuable aid: the spinal fluid will present a lymphocytosis in the former but very rarely in the latter (with the exception of gumma). Besides, the usual course of acquired hydrocephalus in such that is not found in tumors, namely, the symptoms of intracranial pressure, have a tendency to disappear and reappear.

In some cases of serous meningitis the focal symptoms are so pronounced that the diagnosis of tumor strongly forces itself. These cases are the so-called *pseudo-tumors* (Nonne). We may find here cerebellar phenomena, jacksonian attacks, crossed paralysis. But it should be borne in mind that these pseudo-tumors do not possess the characteristic onset and course of the genuine tumors, namely, the continuously progressive evolution of the disease and the early or very early appearance of the local symptoms. In very embarrassing cases, Neisser-Pollack advised a cerebral puncture for the purpose of aspirating the tumor contents. Positive results are, of course, corroborating, but negative ones do not absolutely reject the possibility of pseudo-tumor.

On the previous pages special emphasis was laid upon the early general symptoms of intracranial hypertension, particularly *choked disk*. We must not be unmindful of the fact that tumors situated in certain regions may for a long time present no marked changes in the papilla, especially no choked disk. Such is the case with tumors at the base of the brain, particularly pontine tumors, or tumors of the fourth ventricle or cases of parasitic cysts. In a case of a glioma of the parietal lobe, the writer, after frequent examinations during a period of six months' observation, failed to find other eye-ground changes beyond a slight congestion of retinal vessels until six weeks before death, when choked disk made its appearance. Here again the course of the affection, characterized by a slow but progressive development of the symptoms, besides some general symptoms other than changes in the fundi, will decide the diagnosis.

In recent years *roentgenography* has contributed considerably to the diagnosis of brain neoplasms. Heuer and Dandy,<sup>144</sup> basing their views on a large personal experience, draw the following conclusion concerning x-ray work as an aid in diagnosis of tumor of the brain (1)

With exception of a few cases which show definite tumor shadows, *x-rays* of the head are merely an aid in diagnosis of tumors. (2) Uncalcified tumors do not cast shadows, unless the tumor-tissue has invaded accessory sinuses. As a possible exception may be mentioned hypophyseal lesions which are viewed against dark temporal fossae. (3) Calcified or bony tumors cast shadows which are readily recognized. (4) Signs in skull of increased intracranial tension, i.e., enlargement of the skull, separation of sutures, general convolutional atrophy and destruction of the sella turcica have a considerable value in differentiation between cerebral and subtentorial lesions, for they indicate internal hydrocephalus. It is to be remembered that destruction of the sella turcica may be a general pressure phenomenon. (5) Local changes in the skull due to a tumor are of greatest value in the diagnosis of hypophyseal or suprasellar tumors. The combination of characteristic eye-changes and local destruction or enlargement makes the diagnosis more certain than of any other intracranial conditions. (6) Local hypertrophy of the skull over a cerebral tumor is of a definite diagnostic value. Local atrophy of the skull over the tumor is of equal importance. Local unilateral vascular changes also have a definite diagnostic importance. (7) In about 45 per cent. roentgenography has been of real diagnostic value.

**Etiology of Tumors.**—The causes of brain tumors are, generally speaking, the same as of tumors of any other organ. *Trauma* has been considered as an exciting cause for development of intracranial growths. The symptoms of tumor may begin to appear shortly after the trauma or years later. In such cases if the tumor appears on the site of the cranial trauma, a reasonable connection between the two as cause and effect can be established. It has also been proved that some tumors are of congenital origin, as coexistence of tumors with cerebral malformations has been observed. There are good reasons to believe that glioma is of fetal origin.

In cases of *tuberculous* and *syphilitic* tumors, the cause is evident. Tuberculous tumors are usually secondary to pulmonary affections. Syphilitic growths are acquired after an initial specific infection. Cerebral gummata may occur in childhood upon the basis of hereditary syphilis.

Brain tumors occur more frequently in males than in females. They are particularly frequent in children, although they may occur at any age.

## TREATMENT OF INTRACRANIAL HYPERTENSION AND TUMORS

The syndrome of *increased cerebral pressure*, as we have seen, may prove and disappear spontaneously. This favorable outcome is facilitated by rest, proper **hygienic measures**, **antiluetic treatment** and, in tuberculous cases, by **appropriate management**. In serious cases of hy-



pertension with pronounced symptoms, more **radical measures** are necessary. They are lumbar puncture and surgical intervention.

In *tumors*, **lumbar puncture** is, as a rule, inefficacious and it may be even dangerous. If it is decided upon, it must be done very cautiously, the removal of the fluid must be very slow and, after 1 or 2 c.c. has been removed, the pressure of the fluid must be measured carefully with a manometer. Sicard advises placing the patient with the head low during and for hours after the puncture. Lumbar puncture should never be made when headache and vertigo are aggravated by horizontal position. Lumbar puncture is a useful procedure in serous meningitis (subacute and chronic) by diminishing the stasis of the papilla and improving the symptoms of hypertension. It is, however, ineffectual in localized serous meningitis (cystic).

In such cases, prompt decompressive **craniectomy** is the only treatment, especially when changes in the papilla have been revealed. Excellent results have been obtained. In *brain tumors* this is the only treatment. In some cases the headache is greatly relieved, vomiting disappears and the visual disturbances are much improved. At all events, this operation should be the first stage of surgical intervention with the view of performing later a radical operation for removal of the tumor itself, if possible. This procedure, in view of its safety, is to be advised in the pseudo-tumors. The operation itself consists of removal of a portion of bone usually in the temporal or occipital areas and of opening the dura. In subtentorial tumors it is done in the suboccipital region, in all other cases the temporal region on one, and later on the other side is the seat of choice. The operation should be performed as near as possible to the lesion, so that if subsequently it be decided to attempt the radical operation, there will be less damage to the brain tissue.

In inoperable tumors, when the neoplasm is so situated that it cannot be removed, or when localization is impossible, or when the gravity of the condition is such that delay means loss of sight, **decompression** is urgent and it should be done at the earliest possible moment. While blindness is not prevented in every operated case, nevertheless, the positive results obtained in some are sufficiently striking to warrant the necessity of a decompression. In Cushing's statistics of 130 cases, 59 had increased vision, 65 remained the same, and 16 had decreased vision. Cushing's idea of performing decompression on the side opposite to that occupied by the tumor seems to meet with favor.

If, after decompression, the symptoms of hypertension have not disappeared, **ventricular puncture** should be resorted to through the already existing opening in the cranium. This small operation has proved to be very useful in certain cases of *ependymitis*. Unfortunately, in tumors and even in certain cases of hydrocephalus, the cerebrospinal fluid reaccumulates with rapidity and repetition of the puncture is indicated. On the other hand, repeated traumata of brain tissue lead to small hemorrhages and softening which is certainly a strong contraindication for the procedure. In a number of cases, however, the

removal of about 20-30 c.c. of fluid brings down the ventricular pressure to normal.

Mikulicz recommended **drainage of the lateral ventricles into the subdural spaces**. Since then, various methods of drainage have been advocated. To avoid repetition, the reader is referred to the section on Hydrocephalus.

Finally, Anton and Bramann<sup>145</sup> advocated **puncture of the corpus callosum**. Through a small cranial opening the needle is introduced and it punctures the callosum until the ventricles are reached. The latter are probed, so that any abnormal resistance in them is destroyed. The procedure establishes a free communication between all the ventricles and the subdural space. It relieves promptly the headache, vertigo and vomiting, also the hyperemia and stasis of the papillæ. By preventing rapid blindness, it helps, by gaining time, so as to prepare the patient for an eventual radical operation. The procedure has this advantage, that, in view of the persistence of the opening, a continuous drainage is assured without exposing the patient to septic complications or to hemorrhages.

As to the radical operation for **extirpation of tumors**, it depends upon the seat and character of the mass. From the convexity of the brain, tumors may be removed without difficulty. At the base, only the pontocerebellar tumors offer some chances. Tumors of the brain-stem cannot be touched. Tumors of the hypophysis have been approached with a certain degree of success. Tumors of the posterior cranial fossæ have been removed with considerable success. Soft tumors are less operable than hard tumors. Encapsulated tumors, also cysts, present better results. Metastatic tumors should not be operated upon.

*Complete cures after operations* for cerebral tumors form a very small percentage. In the majority of instances, the substance of the brain remains permanently injured, even after the tumor has been removed. As far as life is concerned, the patients may survive operative procedures for months and even years. In a recent contribution, Keen and Ellis<sup>146</sup> mention the case of a patient who survived for more than thirty years after the removal of a brain tumor. Oppenheim estimates 7 per cent. of lasting success and 7 per cent. with remaining defects.

An analysis of the successes and failures leads to the following conclusions concerning *indications for operative procedures*:

In view of the fact that under complete rest severe symptoms may subside, it is advisable to wait until localization becomes more and more definite or until very important symptoms (such as optic neuritis) make their appearance. On the other hand, immediate operation is indicated when the swelling of the optic disks is increasing and the visual acuity is diminishing, when mental symptoms become more and more accentuated such as hebetude, somnolence and disorientation, when the pain in the head is intolerable, when convulsive attacks become frequent or paralysis more pronounced, finally, when there are present respiratory and cardiac disturbances.

A few words in regard to **medical treatment**: In case of syphilis,

**antiluetic remedies** are indicated. If a gummatous neoplasm is suspected, a trial of these remedies should be given, but only for a short time. *Syphilitic tumors* rarely react satisfactorily to **mercurials**, **iodids** or **arsenphenamin**. In order to avoid the possibility of blindness, time should not be wasted and an operation must be resorted to. The individual distressing symptoms should be treated by appropriate medications, such as **coal-tar products** and **sedatives** for pain, **cod-liver oil**, **iron** and **arsenic** in tuberculous cases. But little is to be expected from medicinal treatment.

### TUMORS OF THE PINEAL BODY

**Anatomical Considerations of the Pineal (Epiphysis).**—The epiphysis is situated beneath and in front of the posterior extremity of the corpus callosum (rostrum) at the level of the posterior angle of the third ventricle between the optic thalami. Below and in front of the epiphysis is the point of communication between the third ventricle and aqueduct of Sylvius. Between the latter and the epiphysis is the posterosuperior portion of the crura. The latter are surmounted by the quadrigeminal bodies with which the epiphysis is in intimate relation. It is placed in the depression between the two anterior quadrigeminal bodies. It is evident that the pineal body is in close relation with several important parts of the central nervous system. In case of increase of volume through a neoplasm or hypertrophy, the gland will obstruct the lumen of the aqueduct over which it lies, interrupt all communications of the cerebrospinal fluid of the third and fourth ventricles, and consequently will produce retention of the fluid in the third and lateral ventricles. The latter will be distended and the surrounding cerebral tissue will be compressed. Moreover, above the epiphysis pass the veins of Galen which carry to the straight sinus the blood from the basal ganglia and choroid plexuses, ventricular walls and the centrum ovale. In case the epiphysis is enlarged, these veins are compressed and the resultant edema still more increases the amount of fluid retained in the ventricles.

The quadrigeminal bodies will then be compressed and their function disturbed: A unilateral lesion of the anterior bodies will cause a bilateral homonymous hemianopsia, a bilateral lesion will produce total blindness (see section on Quadrigeminal Bodies). The compression of the posterior quadrigeminal bodies will result in auditory disturbances. A tumor of the pineal body will interfere with the function of the gray substances surrounding the aqueduct of Sylvius, which contains the nuclei of the third and fourth cranial nerves. The nuclei of the third is composed of several secondary nuclei, each of which innervates one ocular muscle. In case of a partial involvement of the nuclei of the third nerve, one or several ocular muscles will be paralyzed. Tumors of the epiphysis produce also paralysis of associated movements probably because of destruction of the association fibers connecting the nuclei

of both third nerves with each other or with other oculomotor nerves.

Besides the third and fourth nerves, tumor of the epiphysis may involve directly or indirectly the seventh nerve, and, more rarely, the fifth nerve.

The motor tract may be compressed in the foot of the crura, the sensory tract in the tegmentum and especially in the thalamus (its posterior portion particularly).

The cerebellum is involved either in the vermis or in the superior cerebellar peduncles and particularly in the red nucleus.

The rostrum of the corpus callosum is inevitably involved.

The anatomical considerations just described will enable one to construct a clinical picture of various neurological manifestations which a tumor of the pineal body is apt to produce. But there are other symptoms of great importance, somatic, so to speak, which depend upon the function of the gland and which render it characteristic.

**Physiology of the Pineal Body.**—Facts of comparative anatomy, embryology, histology, pathology and experimental physiology tend to prove that the pineal body is a functional organ. It is particularly active from birth to the seventh month. From that time on it shows signs of involution: the number of cells diminishes, the neuroglia proliferates, cysts and calcareous concretions appear in the gland. At puberty it is atrophied. During the period of physiological activity, the gland tends to inhibit the development of sexual function. Consequently interference with the function of the pineal gland may remove, so to speak, a physiological restraint and thus permit a prolonged adolescence or an exaggerated performance on the part of the organs concerned in sexual development.

Sarteschi<sup>147</sup> has succeeded in producing in mammals hypertrophy of the testes and precocious sexual development, also bodily overgrowth by means of pineal extirpation in very young rabbits and puppies. Horrax,<sup>148</sup> by extirpating the pineal gland in guinea-pigs, hastened the development of sexual organs manifested before maturity by a relative increase in size and weight, of testes and seminal vesicles. The pineal-ectomized females showed a tendency to breed earlier than controls of the same age and weight. Horrax expresses the opinion that extirpation of the pineal perhaps produces secondary changes in the hypophysis, which also has an influence over bodily growth and sex development. This view coincides with that of Kidd,<sup>149</sup> who says that the relation of the pineal with the pituitary and adrenal cortex is probable, with thyroid and thymus possible. In view of all these data, the symptomatology of tumors of the epiphysis is of two different orders: symptoms of intracranial hypertension with all the general and local manifestations of a neurological character; (2) symptoms of somatic character relative to the disturbed function of the gland.

**Symptoms.**—I. NERVOUS DISTURBANCES.—As in other cerebral tumor we have here headache, vomiting, vertigo, blindness, convulsions, slow pulse, and mental hebetude. Exceptionally exophthalmos is observed. The reader is referred to the sections on Hydrocephalus and

Tumors of the Brain for a detailed discussion of symptoms common to all varieties of intracranial hypertension. He is also referred to the section of anatomical considerations of the pineal gland to draw conclusions concerning all possible clinical manifestations. A few of these symptoms will be emphasized here.

The *ocular disorders* are the most conspicuous. First of all, congestion, edema and stasis of the papilla and optic atrophy are the rule. The visual acuity gradually diminishes, amblyopia progresses and ends in complete blindness. During the first period of the visual disorder, when the vision is only partly affected, exceptionally hemianopsia is observed because of an involvement of the optic fibers at the level of the pulvinar and external geniculate body. As a rule, optic atrophy occurs before hemianopsia makes its appearance. Ocular palsies are early symptoms and diplopia is common. It is due to a paralysis of one or several muscles of the eye-globe, which may produce all varieties of strabismus. The next important symptom is paralysis of conjugate movements, viz., loss of movements directing the look upward, downward, to the right or left. Pupillary changes are constant. The reactions of the sphincter of the pupil are disturbed because of diminution or loss of vision. Through the anterior quadrigeminal bodies pass sensory fibers which participate in the production of the light reflex; the oculomotor nerve controls the accommodation movements. When these two pathways are destroyed, the light and accommodation reflexes must necessarily be abolished. The pupils may be in a state of mydriasis or myosis, or they may be unequal. Not infrequently nystagmus is observed, being either spontaneous or brought on in lateral movements, this symptom is dependent upon the cerebellum.

Among the *cerebellar manifestations* (see Cerebellar Syndrome) one deserves special emphasis, i.e., the tendency to fall backward, a fact which is probably due to a lesion of the vermis.

*Auditory disturbances* are as frequent as ocular. Although they are present in almost all cases of intracranial hypertension, nevertheless they are more frequent and more intense in tumors of epiphysis because of involvement of the posterior quadrigeminal bodies.

*Motor disturbances* are not pronounced. There is only a unilateral or more frequently a bilateral paresis of the extremities, but no true hemiplegia or diplegia.

*Contractures* are quite frequent. Sometimes they are observed in the upper extremities, but most frequently in the muscles of the neck and opisthotonos has been seen in a large number of cases. Verger observed attacks of opisthotonos. Trismus and difficulty of deglutition are sometimes seen.

The *tendon reflexes* may be normal, but more frequently increased. The toe-phenomenon and ankle-clonus are frequently present on both sides, indicating an involvement of the pyramidal tracts.

*Polyuria* and *polyphagia* are sometimes observed. The sphincters are, as a rule, not involved except in the last phase of the disease when incontinence appears.

**II. SOMATIC SYMPTOMS.**—Tremors of the pineal gland present a special *syndrome concerning a premature development of the body* (see above the physiological considerations). It consists of: (a) rapid growth of the size of the body; (b) rapid development of the external sexual organs; (c) premature appearance of hair on the pubis, in the axillæ and on the face. According to Pellizzi,<sup>150</sup> the syndrome is present before other signs of brain tumor. Bailey and Jelliffe,<sup>151</sup> also Ogle,<sup>152</sup> observed it coinciding with disturbances of the intellect. In Raymond and Claude's case<sup>153</sup> it appeared three years after the headache and vomiting.

The syndrome may be observed complete or else present in only one or two elements.

The increase of size is proportional in all parts of the body. There is a premature although normal ossification (seen by *x-ray*). The cartilages are small, such as are seen in elderly individuals. Dentition, however, does not follow the hastened development; the teeth grow normally. The external genital organs follow the growth of the body. Their aspect is that of the adult organs. The testicles, however, do not develop as much as the penis. Erections and ejaculations are common. Spermatozooids are present in the semen. Pellizzi (*loc. cit.*) observed absence of voluptuous sensations in erections, also that the sexual instinct is not particularly developed. Hair is present on the face and genitalia. The voice is heavy.

The state of *intelligence* is variable. Frequently there is no change, except that depending on intracranial hypertension. In other cases mental feebleness is an early manifestation. (Bailey and Jelliffe, *loc. cit.*) In rare cases (Frankle-Hochwart<sup>154</sup>) it is highly developed.

*Adiposity* was observed in many cases. The pathogenesis of it is still debatable. Some authors, by analogy with hypophyseal tumors, believe that in pineal tumors the hypophysis is compressed by the existing hydrocephalus. In Marburg's case,<sup>155</sup> however, the pituitary was intact and he believes that the adiposity was due to the hyperfunction of the pineal gland. Attempts were also made to explain by secondary disturbance of other ductless glands, but confirmation of these views is lacking. Perhaps the excessive appetite that pineal patients have and the inactivity to which they are usually condemned has something to do with the adiposity.

The *somatic syndrome* is observed in very young individuals below 12 years of age; otherwise speaking, at a period of life when the pineal gland has not finished its total involution. It is considered, therefore, as the result of a disturbance in the secretion of the gland which participates in the nutrition and the metabolism of the body.

**Course and Prognosis.**—The course and duration are variable. The briefest duration of the disease recorded was 3 months, the longest 6 years. Incontinence of sphincters, intellectual feebleness, cachexia, debility, are the habitual manifestations in advanced cases. Coma, elevation of temperature, or else brouchopneumonia announce the approaching termination of life.

**Diagnosis.**—The differential diagnosis between a tumor of the epiphysis and one of the hypophysis is based on the existence of atrophy of the genitalia in the latter. The only common feature between the two is the adiposity. In some cases of hypophyseal tumors there may be acromegaly (Marie) or gigantism (Lannois and Roy). As to the latter, the excessive growth of the body terminates by an abnormal state besides, the genital organs are atrophied—not only the testicles, but also the penis; frequently the pubic hair is absent, the voice remains high pitched, and, in spite of their size, the giants remain infantile.

Apert,<sup>156</sup> and later Gallais, presented a complete description of the so-called *adrenal syndrome* which in some respects reminds of the somatic syndrome of pineal tumors. It is a *genito-adrenal syndrome*. It is met with almost invariably in females. In the latter are seen: hypertrichosis, muscular hyperesthesia, strong sexual instinct, violent disposition, heavy voice and absence of menses. In little girls there develop prematurely secondary sexual characteristics of a masculine type. In man (exceptional occurrence) there is an extraordinary muscular hyperesthesia, and in a boy premature development of secondary sexual characteristics. In all these cases, obesity is pronounced. In differentiating the two syndromes which have in common the adiposity and premature sexual characteristics, one must bear in mind that in the adrenal group the size of the body is not increased, the nervous disturbances are absent, a tumor (hypernephroma) is felt in the hypochondrium. In the epiphysal syndrome, the size of the body is that of an older individual, the sexual instinct is not altered, and there are evidences of a brain tumor.

In ordinary cases of *obesity*, the nervous and somatic syndromes of the pineal tumor are wanting.

As to the DIFFERENTIAL DIAGNOSIS with tumors of the quadrigeminal bodies, the difficulties are in the majority of cases insurmountable.

**Etiology.**—Males are more frequently affected than females. Traumatism, syphilis and other causes observed in cerebral tumors in general are found in pineal tumors as etiological factors.

**Treatment.**—The **palliative** treatment, such as **lumbar puncture** or **cerebral decompression**, as well as the **radical extirpation of brain tumors** in general, can be applied to tumors of the epiphysis.

## C. INFLAMMATION OF THE BRAIN AND BRAIN SHOCK

### ENCEPHALITIS

(*Cerebritis*)

A primary acute inflammation of the brain is a rare affection. It is usually a circumscribed lesion and very frequently leads to suppuration. Trauma is considered one of the causes, but in such cases the

meninges, as well as the brain tissue, are commonly involved, although in rare cases the former escapes. The most frequent cause of primary encephalitis is infection. In the course of infectious diseases, such as diphtheria, erysipelas, scarlet fever, measles, acute tuberculosis, pneumonia, ulcerative endocarditis and whooping-cough, encephalitis may develop. In these cases the inflammation may and may not terminate in suppuration.

#### A. ACUTE NON-SUPPURATIVE ENCEPHALITIS

This variety of encephalitis affects the cerebrum more frequently than the cerebellum. To it belongs the primary cortical cerebritis (polioencephalitis) of the motor area, to which Strümpell first called attention in 1884. He observed it in children and, in his opinion, acute cerebral palsy was due to this cause. A similar condition may occur in the pons, in the gray substance around the aqueduct of Sylvius and is called the "polioencephalitis superior" of Wernicke, to be distinguished from polioencephalitis inferior, or acute bulbar palsy (*see* section on the Medulla).

Apart from these special forms, encephalitis in general has not been classified as a distinct entity. Encephalitis is not uniform in its clinical manifestations. If its seat is exclusively in the central portions, there will be no meningeal alterations and no biological or histological changes in the cerebrospinal fluid. Coma and early paralysis will be the usual symptoms. If encephalitis affects the cortical or ventricular region, the cerebrospinal fluid will not remain intact and convulsive and spastic manifestations will be present. The same phenomena are observed in so-called meningeal reactions. The question naturally arises as to what belongs to the meningeal and what to the encephalic reactions, also what is the relation of encephalic to meningeal lesions, and is there a pure encephalitis or is there rather a meningoencephalitis. In the section on meningeal hemorrhages attention is called to the frequency of simultaneous involvement of the cerebrum and meninges. Autonomy for encephalitis as a morbid entity has always been disputed. In order to determine whether acute encephalitis as an entity is well founded, one must refer to the pathology and etiology.

**Pathology and Etiology.**—The affected area appears swollen and markedly red; its consistency is lessened. The blood-vessels—especially the capillaries—are distended, the foci of hemorrhage are abundant, the nervous tissue and blood-vessels are infiltrated with leukocytes. The brain tissue—fiber, ganglion cells and neuroglia—undergoes degeneration. When the nerve tissue is totally disintegrated, it is eventually absorbed; walls form around the remaining cavity, and a cyst will be the result. The latter may become contracted and a cicatrix develops. Restoration of the affected tissue is rare.

*Histologists* have often found difficulty in distinguishing inflammation from degeneration in nervous tissue. The reason for this lies in the leukocytic infiltration which is seen in the final stage of degeneration.



tion as well as in inflammation. Raymond and Cestan, however, found a positive differentiating sign in perivenous infiltration with round cells. The latter is present without exception in cases of acute encephalitis, but absent in degenerative processes. It is therefore evident that, from the pathological standpoint, autonomy of acute non-suppurative encephalitis is justifiable.

From the *bacteriological* point of view acute encephalitis can claim no specificity. It has been observed in various infectious processes. Chartier<sup>157</sup> injected cultures of various microbes into the carotid artery. Lesions of encephalitis were present, but no microorganisms could be detected in the altered nervous tissue. Only in luetic cases the *Treponema pallida* had been observed in the cerebral tissue as well as in the blood-vessels in cases of encephalitis. Netter reports the case of pneumococcus infection in which the arterioles of the brain contained multiple thrombi. He found the pneumococcus in the intravascular exudates and in the nervous tissue. If microorganisms appear to remain in the blood-vessels, it is logical to assume that their toxins diffused through the vessel walls will affect the surrounding tissue and produce encephalitic alterations—a fact proven by the above experiments of Chartier (*loc. cit.*).

The toxi-infectious etiology of acute encephalitis is thus established.

**Symptoms.**—The relation of the cerebrum to its coverings is so intimate, their contiguity is so perfect and the vascular connections are so absolute that the participation of one in the pathological processes of the other is unavoidable. There may be a difference in the intensity of the lesions of each, but they usually accompany each other.

The symptomatology of encephalitis is rarely characteristic; localizing symptoms are usually wanting, and there are signs of a diffuse cerebral reaction. The frequent coexistence of meningeal lesions complicates the clinical picture.

The symptoms appear *acutely* and the *onset* resembles that of acute infection. Sudden rise of temperature, chills, headache, sometimes vomiting, precede the onset. The disease commences either with convulsions or an apoplectic state or else by a progressive somnolence. When the encephalitis is established, there is a more or less mental hebetude, a more or less marked hypesthesia, a permanent contracture of the limbs, which is from time to time interrupted by convulsive movements. Some rigidity of the neck is common. The pulse is rapid and respiration is of the Cheyne-Stokes type. The special senses may remain intact, but may be also gravely involved, so that amaurosis and deafness may be present.

LOCALIZED SYMPTOMS, if present, will depend upon the seat of the inflammation and, as in the majority of cases, the cortex of the motor area is involved; hemiplegia or monoplegia with local convulsions, with or without aphasia, occur. When death does not supervene during the acute stage, there will be permanent disturbances, the gravity of which depends upon the seat and extent of the lesion. Thus will be observed: palsy of ocular muscles, paralysis of the limbs, hemiplegia or diplegia.

ataxia, athetosis, nystagmus, speech disturbances, mental deficiency, arrest of development and epilepsy.

Besides this grave form of encephalitis there are also mild and very mild forms. All degrees may be encountered between the two extremes; they depend upon the intensity of the pathological process.

**ACUTE ATAXIA.**—A special symptom-group of more or less complexity has been observed in some cases of acute encephalitis. It is known under the name of *acute ataxia* and was first described by Leyden in 1868. Its various manifestations may be all present at the same time or else they may succeed each other. They consist of disturbances of the motor apparatus, of the speech and of intelligence.

(a) *Motor Disturbances.*—Disequilibration is a predominant symptom. Incoördination, ataxia, dysmetria, choreiform movements, athetosis and tremor are its characteristic symptoms. Not only station and gait, but also the handling of objects and the act of writing are affected. Muscular force is preserved, and if paralysis appears it rapidly disappears. These symptoms are irregularly distributed. The sphincters are usually intact, except in the beginning. The tendon reflexes are increased, ankle-clonus and toe-phenomenon are present.

(b) *Speech Disturbances.*—The speech disturbances resemble those which are observed in cerebellar atrophy and disseminated sclerosis. The speech is scanning, each syllable is pronounced in an explosive manner or in a hesitating manner (André-Thomas).

(c) *Mental Disturbances.*—Changes of disposition, irritability, loss of memory, crying and laughing without a cause, confusion and diminution of intelligence are the symptoms observed. It is evident that here the entire cerebrospinal axis is involved. When the cerebral symptoms predominate, there will be mental confusion and hemiplegia; when the cerebellar symptoms predominate, there will be asynergia, ataxia, catatonia and nystagmus; when the spinal symptoms predominate, the reflexes and sphincters will be altered.

In spite of the gravity of the condition, acute ataxia may improve and even disappear. But even in the most favorable cases some permanent traces will be observed, such as nystagmus, increased reflexes, and toe phenomenon.

This affection, which belongs to the group of non-suppurative acute encephalitis, is met with only in young individuals. It is of infectious origin. It has been observed in small-pox, diphtheria, measles, erysipelas, influenza and pneumonia. The cerebrospinal fluid shows albuminosis and lymphocytosis. In the few cases that have come to autopsy, diffuse or disseminated lesions of encephalomyelitis were found.

The identity of acute ataxia with acute encephalitis and meningo-encephalitis, from the standpoint of pathology and etiology, is complete. The only difference lies in the intensity of the symptoms.

**Prognosis.**—During the comatose state the outlook is usually unfavorable. Death may occur in twenty-four hours. The severity of the prodromal symptoms and the degree of the coma generally determine the prognosis in a given case; after the acute symptoms subside, the

prognosis is more favorable. Recovery without some defect is rare. Focal epilepsy, impaired speech and some paralytic condition of one or two limbs on the same side of the body are the most frequent sequelae of acute encephalitis.

**Treatment.**—During the acute stage applications of **ice to the head**, and **bleeding** in addition to **absolute rest**, are practically the only measures that can be recommended. If the fever is very high, **antipyretics** should be used. The treatment of the chronic stage is identical with that of the chronic stage of apoplexy.

## B. ACUTE SUPPURATIVE ENCEPHALITIS

### *(Abscess of the Brain)*

**Etiology.**—The most constant cause of acute encephalitis terminating in suppuration is a lesion of the bony walls of the cranium. Trauma of the scalp, of the meninges and of the brain tissue may also be followed by the formation of an abscess. In connection with this factor it should be borne in mind that in some cases abscesses of the brain were observed long after the occurrence of the trauma, also that in certain groups of cases the trauma of the head was slight and still suppuration developed in the brain.

A metastatic embolus originating in some purulent focus of the body, like cellulitis, abscess of the liver, purulent processes in the bronchi or lungs, or other viscera, is another cause of abscess of the brain. Suppuration of the mucous membranes lining the cavities of the cranium (nose and accessory cavities) is the third cause of abscess.

Finally, the most important and most frequent cause of abscess of the brain is *otitis media* and especially its chronic form (90 per cent.). Small veins and lymphatics pass from the tympanum to the superior petrosal sinus; similar vessels end in the same sinus from the temporosphenoidal lobe of the brain. Identical vessels come from the lateral lobe of the cerebellum and from the mastoid region, and all end in the lateral sinus. The channels of infection are thus explained. Diseases of the ear are apt, therefore, to produce an abscess in the temporosphenoidal lobe and in the lateral lobe of the cerebellum.

If the abscess is caused by diseases of the nasal cavity, the abscess is situated in the frontal lobe. The infection is carried through the venous and lymphatic channels or directly from the carious bone. Whatever the original cause may be, suppuration in the brain necessitates the presence of multiple microorganisms, among which the streptococcus plays the most important part. A rare variety is the cerebral suppuration in which the tubercle bacillus alone was found (Fraenkel, Rendu and Boulluche). The infection may be transferred to the brain tissue, either through the venous sinuses—which are then in a state of inflammation—or through the arterial system. The latter will occur in those cases in which the initial purulent focus is far away

from the brain; the former will take place when the suppuration is in proximity to the brain.

As to the seat of the abscess, it is most frequent in the hemispheres, rarely in the basal ganglia; the metastatic form is in the area of distribution of the middle meningeal artery; the otitic form has its seat in the temporosphenoidal lobe or cerebellum; the traumatic form is usually confined to the injured region of the cranium.

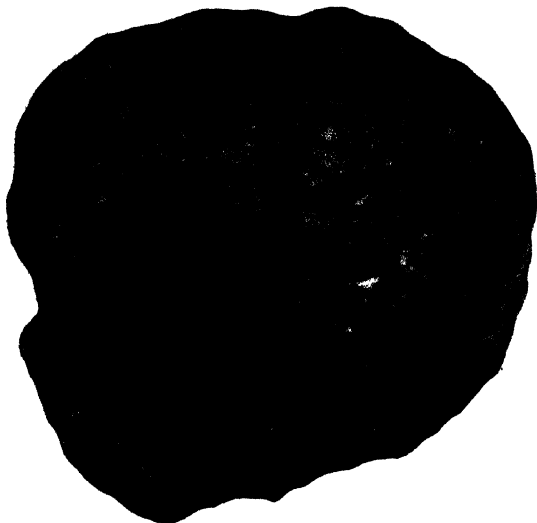


FIG. 16.—ABSCESS IN RIGHT FRONTAL LOBE.  
(Gordon, Courtesy *Journal of Nervous and Mental Diseases*.)

The average age at which cerebral abscess is met with is between twenty-five and forty years; it is rare above sixty. Males are more frequently affected than females.

**Pathology.**—Two principal conditions are to be considered. In one there is a purulent infiltration with softening of the cerebral tissue; another is characterized by formation of a circumscribed abscess which becomes encapsulated. In the latter case the capsule is formed of the connective tissue of the blood-vessels; its formation commences, according to Cassirer, on the eighth to the tenth day, and, according to Friedmann, on the fifth day. If the capsule is complete, it furnishes protection to the surrounding nervous tissue against invasion of pus, but not infrequently fistulous channels are to be found, and the formation of pus continues indefinitely. As to the capsule itself, it is thin at the

beginning; later it grows thick and may become calcified. While it is thin, pus is apt to rupture it. When the rupture occurs on the surface of the brain, purulent meningitis will be the result. When the pus breaks through the capsule into the ventricles sudden death may follow.

Single encapsulated abscesses are met with in the majority of cases, but multiple abscesses may also occur, especially in the metastatic form and in general pyemia. The brain tissue in both cases—namely, in purulent infiltration and abscess—undergoes at first “red softening” in which disintegrated nerve elements, leukocytes and microorganisms, are found. The exodus of leukocytes from the vessels is extensive and rapid: they surround the blood-vessels and the nerve tissue which is softened and edematous. Cells and nerve fibers are destroyed and replaced by pus. The immediate vicinity of the abscess is softened.

**Symptoms.**—The clinical manifestations are general and local.

The onset of acute suppurative encephalitis is similar to that of tubercular meningitis in children. Fever is the first symptom to appear, but it is not pronounced. What is often observed is a lack of parallelism between the pulse and fever: while the latter is high the pulse may be slow. Soon violent headache sets in. The patient becomes restless, agitated, cannot sleep, refuses food, and has attacks of vomiting. The headache is continuous. The localized headache and exacerbation on the slightest movement of the head make it typical of acute suppurative encephalitis. In cerebellar abscess the pain is mostly in the occipital region. Pain is frequently present at the seat of the abscess, and if pressure or percussion of this region is particularly painful, the pain may have a localizing value, especially if it is elicited in the temporo-sphenoidal region. As the disease advances, delirium and generalized convulsions make their appearance. Convulsions are frequently an indication of accompanying meningitis or sinus phlebitis. Rigidity of the neck, photophobia, and ocular palsy then make their appearance. Optic neuritis at times is seen early in the acute stage. Mental hebetude and apathy are conspicuous.

In the second phase of the disease the above symptoms are much ameliorated. The fever may be normal or even subnormal. It is important to bear in mind that in a very considerable number of cases there may be no fever at all during almost the entire course of the disease and that, therefore, absence of fever would not argue against the possibility of a cerebral abscess.

The amelioration of the symptoms does not last any marked length of time. Soon a state of apoplexy follows. The coma may be so profound that the patient will not regain consciousness and will die. If he happens to recover, there will be present unilateral motor and sensory disturbances, such as rigidity, paralysis, aphasia, blindness, hemianopia, etc. They depend upon the area of the brain involved.

The local symptoms are identical with those of brain tumor. The further evolution of the disease will depend upon its anatomical course. If the abscess breaks into the ventricles, death will ensue. Some cases run such a rapid course that fatal termination may take place in a day.

short time. In the course of some cases of cerebral abscess associated with otorrhea the discharge may repeatedly stop. At each stoppage there is a marked aggravation of headache. It is due to increase of intracranial pressure. The reestablishment of otorrhea relieves the symptoms.

In a certain number of cases with a history of trauma or old otitis, in which the abscess remains latent for months and even years without being suspected, death takes place either from rupture of the abscess or from an acutely developed morbid process in, or in the vicinity of, the abscess. This is the so-called *latent form*. To the same group belong those cases in which the abscess is seated in the depth of the frontal lobe or in the postero-external portion of the occipital lobe. In such cases there are very few symptoms; sudden death is the usual result. However, the *latent form* may sometimes end gradually: an intercurrent acute meningitis may aggravate the few existing symptoms which continue then to increase until death.

**Prognosis.**—Generally speaking, the outlook is grave. In chronic and subacute cases the prognosis is more favorable than in the acute cases. Complete recoveries have been reported by some writers, especially in uncomplicated cases and in those that were operated upon early. In the latent cases the abscess may remain encapsulated for a long time without producing serious disturbances, but the patient is always threatened with complications such as meningitis and edema of the brain.

**Diagnosis.**—In the *traumatic cases* the diagnosis is not difficult when the signs of cerebral abscess develop parallel with the cranial injury, but it is difficult when the symptoms develop without an evident injury to the skull or some time after complete healing of the injury. In such cases abscess should be thought of when general and local symptoms appear after a trauma of the skull.

Traumatism of the cranium is liable to develop a *hemorrhagic pachymeningitis*. The distinguishing symptoms between it and cerebral abscess are: the onset of hematoma directly after a trauma, the character of pain which is superficial and not augmented by motion in hematoma, and finally the duration of fever, which is only transitory in abscess but not in hematoma.

A cerebral abscess caused by *otitis media* is recognized without special difficulty when, in the course of the latter, a localized palsy affecting one or two extremities makes its appearance. A septic otorrhea and perforation of the tympanum are in favor of cerebral abscess. Absence of perforation also speaks for brain abscess. In cases of suspected abscess with otitis it is important to know whether the abscess is in the temporo-sphenoidal lobe or in the cerebellum. Pronounced occipital headache with symptoms of cerebellar syndrome (*see* this section) will enable one to make the differential diagnosis. Distinct, even though slight, symptoms of **low-grade aphasia and paraphasia** are undoubted symptoms of temporal abscess on the left side in right handed individuals. Right-sided temporal lobe abscess can be recognized only by its neighborhood

symptoms, i.e., oculomotor disturbances, hemianopsia and paresis on the opposite side.

Next to the otogenic abscesses the *rhinogenic* should be considered. Not only the ear, but also the nose and orbit should be examined in every case. Frontal headache should arouse suspicion, as local symptoms are rarely present. Even general symptoms are frequently absent in frontal abscesses. However, absence of abdominal reflexes on one side points to an abscess in the frontal region. *Sinus phlebitis* will be recognized by high temperature, rapid pulse, chills, sweating, and particularly by tenderness and swelling over the origin of the internal jugular vein.

*Meningitis* may be confounded with abscess, but the rapid onset, involvement of the cranial nerves, high temperature, rapid and irregular pulse, are all rarely found in abscess. Lymphocytosis with turbidity, also high pressure of the spinal fluid, are in favor of purulent meningitis. Increased pressure, lymphocytosis and clear spinal fluid are in favor of serous meningitis. Increased pressure without lymphocytosis very frequently speaks for abscess (and tumor). In children *tuberculous meningitis* will be recognized by the rigidity of the neck, attacks of focal epilepsy or of paralysis, elevation of temperature and the above condition of the spinal fluid.

*Tumor* of the brain will be diagnosticated by its uniformly progressive course and very much prolonged duration. Convulsions, if they occur, are more frequent and more regular than in abscess. Headache is more progressive, more severe and longer in duration in tumor than in abscess. Involvement of cranial nerves, and especially double optic neuritis and atrophy, are common in tumor and exceptionally rare in abscess. A unilateral optic neuritis is in favor of abscess. The sudden appearance of symptoms of meningitis or of sinus phlebitis is an indication of abscess. Leukocytosis is also in favor of abscess.

When there is no external evidence of injury, or of bone or ear disease, *metastatic* origin of cerebral abscess should be thought of. Heart, lung and other viscera must be carefully examined.

**Treatment.**—Prevention of formation of cerebral abscess can be carried out by paying careful attention to all cranial injuries, by guarding against infection and by thorough treatment of ear suppuration, no matter how slight the latter may be. As soon as strong suspicion of abscess is present, prompt **surgical intervention** should be the only treatment. In obscure cases, in which but a very few symptoms are evident, palliative measures may be applied for a short time, viz., **counterirritation**, **local bleeding**, application of **ice** to the painful region, **purgation**, **sedatives** to allay excitement, **stimulants** to combat depression. If there is no marked improvement, **operation** must be promptly resorted to. Statistics show that early surgical intervention is responsible for a large percentage of recoveries, but these occur by no means in every case, even if performed at the right time and if complications do not occur. The reason for failure probably lies in the fact that the entire abscess could not be evacuated, or that there are other abscesses, or that the area of softening around the abscess is very extensive.

Cerebellar abscess is, from the operative standpoint, less favorable than cerebral abscess. As to the seat of the operative field, the surgeon has to be guided by localizing symptoms (*see Cerebral Localizations*).

### C. CHRONIC ENCEPHALITIS

#### (*Cerebral Paralysis of Children*)

As a primary affection chronic encephalitis is very rare in adults. It is observed as isolated foci in multiple sclerosis, in the vicinity of tumors and in old syphilitic cases. In a diffuse form it is encountered in paresis in association with meningitis (meningo-encephalitis).

In children chronic encephalitis presents special features. It is the final stage of disease processes which differ from each other in regard to the morbid anatomy and etiology but have one factor in common, namely, that they affect the brain during fetal life or in early infancy. The existence of this condition, although well known before Chareot, was ignored until Strümpell called attention to the polio-encephalitis of infancy. Lallemand, in 1834, had shown that various forms of malformation of the brain (agenesis) were the result of encephalitis. This view was corroborated by Chareot and especially by Bourneville who had great opportunities of dealing with idiots and defective children and of verifying the clinical symptoms by anatomical findings.

There are two special forms of cerebral paralysis of children: *spastic infantile hemiplegia* and *Little's disease* (diplegia, paraplegia).

**Etiology.**—Trauma of the gravid uterus, trauma of the cranium of the fetus during difficult and protracted labor, with or without instrumental delivery, may produce meningeal hemorrhages which injure the motor cerebral centers and cause unilateral or bilateral lesions. Experience teaches that abnormal conditions which lead to long and difficult labor are more apt to produce birth paralysis than proper application of instruments.

Little (1862) lays special emphasis on *dystocia* and especially on *premature birth*. The fact that many children, prematurely born, show cerebral changes which could be traced to a date long before birth, is suggestive of the possibility that the causes which underlie premature birth are at the same time the causes of cerebral paralysis, such as syphilis, for example.

*Infectious diseases* are important etiological factors. The disease occurs in the course of measles, scarlet fever, typhoid, diphtheria, whooping-cough, or mumps. Strümpell's polio-encephalitis of infancy belongs to this class. The hemiplegic form is more frequently acquired than the congenital. Whether it is due to the infectious element itself or to an embolism or venous thrombosis (Gowers) or to a hemorrhagic influence in the motor area, it is difficult to say.

*Syphilis* may play a predominant rôle in the congenital and post-natal cases. Fournier considers the paraplegic type as a parasymphilitic affection.



*Psychoses and nervous diseases, phthisis and alcoholism* in the family of preceding generations may be considered as predisposing factors. Bournville's researches show that parental alcoholism showed its effect in 41 per cent. of cases. Finally chronic metallic *intoxications*, lead, mercury, and phosphorus, have also been mentioned as causes of infantile encephalopathies.

*Meningeal hemorrhages during birth* deserve special mention. Not only will traumatism during labor produce hemorrhages but spontaneous hemorrhages may also occur in the fetus. The latter are due to a special fragility of the blood-vessels, especially the veins—fragility which is due to hereditary syphilis, alcohol, lead intoxication or to debility from any cause. The largest of the subarachnoid veins which are usually ruptured, are located along the anterior and posterior borders of the parietal bone, which correspond to the lambdoid and coronary sutures. The coronary suture corresponds to the rolandic area, and consequently a hemorrhage at this level produces motor symptoms. This is ordinarily the case. These are hemiplegia, monoplegia, tremor and convulsions. If convulsions do not disappear the following manifestations will eventually be observed: arrested mental development, Little's disease, disturbance of vision, ocular palsies, deafness, various malformations in the limbs and disturbance of speech. It is therefore evident that the recognition of meningeal hemorrhages in newly born infants is a matter of great importance. As soon as they are recognized, operative procedures become urgent (*see* section on Meningeal Hemorrhages).

**Pathology.**—The anatomical findings in the brain are various. Lesions caused by vascular disorders are in the majority; foci of softening or hemorrhage are frequent. Evidences of inflammatory processes are next in frequency, but primary degenerative processes are in the minority.

Evidences of chronic meningitis are frequently seen with the naked eye. The peculiarity which is characteristic of chronic encephalitis in children lies in the retraction of brain tissue around the old morbid foci. The retracted nervous tissue forms a depression, yellow in color (yellow plaques), especially noticeable in the motor area. The thickened dura is adherent to the convolutions. The cortex undergoes changes; cells and nerve fibers are in a state of degeneration. Briefly speaking, the condition is one of a meningo-encephalitis.

Old lesions may lead to special cerebral defects, called *porencephaly*. The latter is characterized by deep, funnel-like depressions. The depth of the depressions is various. They may involve only a small portion of brain tissue or communicate with the lateral ventricles, may be unilateral or bilateral and show a predilection for localization in the region of the motor centers, also the third frontal and first temporal convolutions. They have always been observed in areas having a well-defined arterial supply. This led to the view that a vascular influence is the cause of porencephaly and that destruction due to a hemorrhage or softening will produce a depression; in this case the depression or cavity does not reach the ventricle.

An old lesion in the form of an inflammation limited to the walls of the lateral ventricles, involving the ependyma, leads to another peculiarity, i.e., *internal hydrocephalus*. It is characterized by a considerable accumulation of fluid in the ventricles. The cerebral tissue which is in immediate contact with the walls of the ventricle is destroyed, and the convolutions being under continuous pressure, become atrophied.

*Atrophy of brain tissue* was also observed in a number of cases as the result of a primary sclerotic process which may develop from hemorrhage, thrombosis, or encephalitis. The condition usually affects an entire cerebral hemisphere. The convolutions are found thin, retracted, indurated, and lighter in color than normal cerebral tissue. It may happen that only one or several lobes of the same hemisphere are affected



FIG. 17.—PORENCEPHALY (PEEBLE-MINDEDNESS; EPILEPSY).

(From Gordon's "Diseases of the Nervous System," P. Blakiston's Son & Co.)

(*microgyria*). The microscopical lesion consists of a marked proliferation of neuroglia, also of a thickening of the walls of the capillaries and multiplication of the latter. The retraction of the newly formed fibrous tissue leads to a dilatation of the perivascular spaces. These changes are present in the gray as well as in the white matter, though more marked in the former than in the latter; the cells gradually change their form and finally disappear. Instead of atrophic sclerosis the brain may present a *hypertrophy* of some of its parts. Sometimes large parts of the brain show signs of induration or there exist bulb-like indurations (tuberous sclerosis). As to the cause of cerebral sclerosis, it is generally admitted, with Virchow, to be due to a *congenital chronic encephalitis* in which all the elements of the cerebral tissue are affected.

Of special interest with regard to the pathological physiology of muscular rigidity is the condition of the pyramidal tract. In the fetus or in early infancy the latter is not yet completely developed, as the myelin covering the axis-cylinders begins to appear only during the first

months after birth. It stands to reason that a lesion in the brain at those periods of life leads to an arrest of development and atrophy of the portions of the nervous tissue beneath the initial lesion. Atrophy and



FIG. 18.—INFANTILE CEREBRAL HEMIPLEGIA.

(From Gordon's "Diseases of the Nervous System," P. Blakiston's Son & Co.)

diminution in size of nervous tissue (brain and cord) are therefore characteristic of the lesions in question.

**Symptomatology.**—A. INFANTILE SPASTIC HEMIPLEGIA.—The largest majority of cases are postnatal and originate in the first three years of

life, although congenital cases, or such as have their origin during delivery, are not rare.

The disease is usually ushered in by fever, restlessness and vomiting. Convulsions appear early if not first; they are epileptiform and are confined to the side which is to become paralyzed. The spasms soon become generalized and increase in frequency. During the epileptic seizures which usually last about forty-eight hours, the hemiplegia suddenly sets in. Sometimes the first attack leaves only slight motor disturbances, which after each subsequent attack become more and more pronounced, until a complete hemiplegia occurs.

The paralysis of sudden onset is at first flaccid, and affects the arm, leg and face; the distal ends of the extremities are the most affected, and the upper extremity more than the lower. At the end of ten to fifteen days spasticity gradually develops, all the reflexes become exaggerated, and ankle-clonus and the toe-phenomenon are easily elicited. The hemiplegia is established and remains permanent. While in a general way it is similar to the hemiplegia of adults, it nevertheless presents one peculiarity, namely, that the contractures with subsequent deformities are very marked. The contractures are most pronounced in single groups of muscles, especially in the flexors and pronators of the arm, and in the flexors of the leg. For this reason the following flexed positions are produced: the arm is flexed at the elbow and held tightly against the body; the hand is flexed; the thumb is turned inside the closed fist; the leg is flexed and rotated inward; the foot is in the varus equinus position; and the great toe is extended dorsally.

The paralyzed limbs are frequently affected with posthemiplegic *volitional* and *spontaneous movements*. Spastic innervation in voluntary movements is sometimes striking. It consists of *intention spasms*. The latter interfere with every action and the more intense the exertion the stronger the inhibition. The retarded and interfered movements are the result of constant efforts of the patient to control the inner resistance. This condition is quite characteristic of the disease. The spastic nature of the volitional movements is frequently accompanied by *ataxia*. *Associated movements* are frequent. (For details see section on Hemiplegia in Adults.)

The *spontaneous movements* are chorea and athetosis on the hemiplegic side. The choreic movements are seen mostly in the upper extremity and sometimes in the face, but athetosis is seen in the fingers and toes. In the face grinnacing is not infrequent. The less the paralysis is marked, the more intense and extensive are the spontaneous movements. Occasionally both varieties of movements are combined. In some cases there is an *intention tremor*, such as is seen in disseminated sclerosis. All spontaneous movements disappear during sleep, with the exception of very severe cases of athetosis.

Disturbances of *sensations* are rare. Astereognosis is occasionally observed, probably because the tactile memory pictures have not yet been acquired at the time—in very early life. Special sensations some-

times present defects, such as strabismus, hemianopsia, nystagmus, and deafness.

Another conspicuous feature of infantile spastic hemiplegia is *atrophy* of the paralyzed side: skin, fat, connective tissue, musculature and bone participate in the atrophic process; not only the limbs but the



FIG. 19.—DIPLEGIA (LITTLE'S DISEASE).

(From Gordon's, "Diseases of the Nervous System," P. Blakiston's Son & Co.)

face and thorax show diminution in size. Deformity of the skeleton, particularly scoliosis, is observed. The atrophy is more marked in the upper extremity than in the lower. The skull frequently shows asymmetry and flattening of the parietal bone.

There are *vasomotor disturbances* present: the skin is cold on the affected side.

*Aphasia* is an exceptional occurrence. More frequently there is a delayed development of speech faculty.

Of great importance in their bearing on later life are *disturbances of intellect* and *epilepsy*. The former are more frequently met with when the frontal lobe is congenitally diseased than the rolandic area. In view of the tender age of the child there is a retardation of mental



FIG. 20.—LITTLE'S DISEASE.

(From Gordon's "Diseases of the Nervous System," P. Blakiston's Son & Co.)

development in almost every case. Imbecility and idiocy are observed in some cases. Only in a minority of cases are the mental faculties preserved, but even in those there is change of character, viz., irritability and a tendency to outbursts of anger. Epilepsy is a frequent complication. It may exist from early infancy or make its appearance later, especially around puberty. The convulsions may be confined to the paralyzed side or may be generalized. In many cases the epilepsy has a tendency to decrease with age, but in others to remain permanently. According to Bourneville, severe epileptic attacks last usually from ten to fifteen years, after which period they become mild and may

disappear in middle age. Petit mal attacks or psychic equivalents occur usually in cases in which the paralysis is slight.

B. SPASTIC DIPLEGIA: LITTLE'S DISEASE.—In the section on Pathology a description was given of the various morbid conditions which are apt to create the paralytic states observed during life. When the lesion,



FIG. 21.—MICROCEPHALY AND DIPLEGIA (IDIOT).

instead of being unilateral, is symmetrically distributed to the motor areas of both hemispheres, the clinical manifestations will be *double hemiplegia* or *diplegia*. When the lesion affects the paracentral lobule, a paralysis of both lower extremities will be observed (*paraplegia*). Spastic diplegia and paraplegia may be observed in two different conditions: *congenital* and *acquired*. Feer and Freund believe that asphyxia and difficult labor are mostly found in the history of diplegics, premature birth usually in that of spastic paraplegia.

In the section on the etiology of chronic encephalitis mention was

made of premature labor as being the chief cause of the disease. It was also pointed out that in many cases hereditary syphilis is the cause of premature labor and Little's disease. Not infrequently diplegic children present certain stigmata of syphilis, such as hydrocephalus, internal strabismus, etc. In some cases at autopsy lesions of syphilitic nature have been found: sclerotic and gummatous formations, meningeal conditions, cerebral endarteritis, and meningomyelitis. Finally, the Wassermann reaction has been frequently found positive in diplegics. Writers are divided in their conclusions on this subject: Some describe, under the name of Little's disease, both the congenital and the acquired forms; some make a sharp distinction and consider three characteristic features necessary for Little's disease, viz., (1) the affection must be congenital, (2) it must be of cerebral origin, and (3) it must be due to agenesis of the pyramidal tract.

In the section on Pathology an explanation was presented concerning the pathogenesis of the spasticity in the congenital cases. It was said that in view of absence of myelin in the nerve fibers during the first months of life, also in view of lack of full development of the pyramidal fibers up to the seventh month of life (they are present only in the brain and medulla, but absent in the spinal cord [Van Gehuchten])—for all these reasons there cannot be a continuity between the cortex, which sends out stimulation, and the peripheral nerves. Therefore, the stimulation sent out from the cortex to the spinal centers is not properly transmitted for want of pyramidal fibers. The rigidity of the muscles is due either to an increase of muscular tonus or to transmission of continuous morbid stimulation through imperfectly developed pyramidal fibers.

**SYMPTOMS OF PARAPLEGIC FORM.**—The most frequent variety is the *paraplegic*. The gait and station are characteristic: the trunk is bent forward, the patient looks at his feet, the latter are in a state of varo-equinus. When standing, the thighs are in close contact with each other because of spasm in the adductors, while the legs are separated. In walking, the knees constantly rub one another and the legs cross each other. The feet, in standing, touch the ground only with the tips of the toes, in walking they make a semicircular movement and scrape the floor at each attempt to advance, and the trunk turns laterally. When seated, the legs do not touch the floor; they are extended; the great toes are also in a state of extension. When walking is possible, each attempt is accompanied by an effort to overcome an *internal resistance* and the whole trunk is stiffened like a board (*see Intension Spasm in section on Infantile Hemiplegia*).

**SYMPTOMS OF THE DIPLEGIC FORM.**—In the *diplegic* form the upper extremities are also affected, but to a milder degree. Adduction of the arms, flexion and pronation of the forearms are the principal signs. When the face participates in the general rigidity, it assumes a mask-like expression. When the patient speaks, laughs or masticates, there is a very marked contortion of the muscles of the face; the speech is therefore indistinct and words are pronounced in an explosive manner. Should



the muscles of deglutition, phonation or respiration be involved, congenital pseudobulbar paralysis will be present.

Choreic movements are not frequent, but athetosis is not infrequently observed in both hands. The condition of the reflexes is the same as in the hemiplegic form.

The cranial nerves are not infrequently involved. Strabismus and nystagmus are not rare. Occasionally optic atrophy is observed. König called attention to "changing pupils," i.e., pupils are unequal and the inequality changes from day to day. Epilepsy is very frequent, especially in diplegia associated with idiocy and imbecility.

The mental condition deserves special mention. While the children thus affected present some delay in development of their mental faculties, they nevertheless do not show marked impairment of intelligence, and in some cases with proper training their intellect may reach a normal degree of development. There are also cases of diplegia in which idiocy and imbecility are observed, especially cases with grave malformations of the brain as the result of prenatal disturbances in development. In cases due to traumatism during delivery the mental faculty is often badly impaired.

Diplegies not infrequently present a peculiar excitability in regard to noises; this is what Oppenheim called "abnorme Schreckhaftigkeit." When they hear an object fall on the floor or hear a noise of any sort, they are seized with a trembling which may last a long time. The condition is an acustico-motor hyperesthesia. The same author also called attention to the so-called "eating reflex." It consists of rhythmical chewing, sucking and swallowing movements upon stroking the lips or the tongue.

**Prognosis.**—Generally speaking it is unfavorable. Contractures, atrophy, arrested development of the tissues of palsied limbs, render the infirmity permanent. Epilepsy is a very grave complication, as it prevents any possible amelioration of symptoms and retards the development of mental faculties. The development of mental faculties is usually delayed, but with proper training good results may be obtained. In diplegia there is a natural tendency toward improvement, but recovery can never be expected.

**Diagnosis.**—Spasticity of the paralyzed limbs, marked contractures, athetosis and chorea with epileptiform convulsions, and the period of life at which these symptoms make their appearance are usually sufficient facts for making a diagnosis. In some cases, however, difficulties arise. When infantile spastic hemiplegia presents an acute onset, the character of the disease cannot be recognized before the appearance of paralysis. In such cases the disease may simulate *tubercular meningitis*. The course of the affection alone will prevent an error in the diagnosis.

*Infantile spinal paralysis* will be recognized by the flaccidity of the palsy besides the diminution or loss of reflexes.

*Obstetrical palsy*, limited usually to one upper extremity, can be recognized by its flaccidity.

*Tumor of the brain* gives a history of slow onset, of headache, vertigo, optic neuritis or atrophy, or choked disc.

*Hydrocephalus* is recognized by the size of the cranium and the appearance of disturbances in the optic nerve.

The paraplegic variety of Little's disease will be differentiated from paraplegia caused by myelitis mainly by the absence of disturbances of the sphincters, but also by the history of the case.

Under the names of Cerebrocerebellar Diplegia, Cerebrocerebellar Ataxia, Atonic Form of Cerebral Diplegia has been described a special syndrome in which cerebral as well as cerebellar symptoms are simultaneously present. The reader is referred to the section on the Cerebellum.

**Treatment.**—In the section on Etiology dystocia and protracted labor were considered as important factors. It is therefore evident that prompt obstetrical intervention during difficult labor is an important prophylactic measure. When hemiplegia, preceded by a group of acute symptoms, appears some time after birth, the treatment will not be different from that of an apoplectic stroke in an adult. It is the treatment of deformities and infirmities that we are requested to remedy. **Internal drugs are of no value except for epileptiform convulsions**, in which case the treatment of epilepsy in general is appropriate. Should the convulsions be focal, surgical procedures may be attempted for removal of scars or for evacuation of cysts.

The relation of diplegia to hereditary syphilis (*see above*) is a sufficient justification for the use of **antiluetic remedies**.

**Mechanical means and surgical intervention** are the only possible means of treatment. It is well understood that conditions like porencephaly, internal hydrocephalus, sclerosis and atrophy of the brain can never be benefited by operative procedures on the cerebrum. When the paralytic or epileptic symptoms are due to a vascular lesion or to a cyst, some improvement may be expected, but not a permanent recovery. Statistics show that in a certain group of cases some improvement was obtained but it was only temporary; also a number of fatal results were recorded. However, more recent investigations—especially those of Cushing—show that in many cases congenital paralysis is due to hemorrhages within the cranium at birth (*see Meningeal Hemorrhage in Infants*). Prompt and early surgical intervention for removal of blood-clots may give very satisfactory results. In view of the great gravity of such operations in newly born infants Gilles devised a method which apparently gives promising results. This rule is first to perform a **lumbar puncture**, and when the latter gives no relief, the **anterior fontanel should be punctured**. This decreases intracranial pressure and reduces the danger of infection caused by absorption of toxic products from the blood-clot. The punctures are, in Gilles' opinion, a preparatory treatment. When the brain becomes more developed and the child is stronger, a **radical operation** may be undertaken.

Surgery directed toward the deformities and contractures is apt to give favorable results. **Tenotomy and myotomy** followed by the appli-

**cation of plaster casts to the limbs**, to put them in corrected positions, have given favorable results in certain cases. Through **transplantation of tendons** hypertonic muscles are carried to regions where the function of the muscles is impaired, so that chorea and athetosis in some cases greatly improved and even disappeared. Various **orthopedic appliances, passive manipulation of limbs, mobilization of joints and properly regulated gymnastics** are highly commendable for counteracting the rigidity of the muscles and of their tendons. Sachs reports permanent cures of athetoid movements through wearing an **apparatus of splints** for several months which made these movements impossible. **Massage** is a great adjuvant in the treatment, as it tones down the rigidity of the muscles. **Warm baths** facilitate the reduction of muscular rigidity. **Electricity** is not advisable, as it is likely to increase the spasticity.

Recently Förster<sup>158</sup> has suggested resection of the posterior spinal nerve roots for relief of spasticity. He based this operation on the following physiological considerations: Spastic paralysis is due to a diseased condition of the corticospinal tract, especially the pyramidal tract. The latter carries two kinds of fibers: those bearing the motor impulse, a morbid condition of which causes the paralysis, also those containing inhibitory fibers whose function is to check the sensory stimuli received from the sensory roots of the spinal cord. The spasticity is therefore a reflex act. As a result of the damage to the inhibitory fibers the continuous sensory impulses act unrestrained—hence the spasticity.

When, in such cases, the posterior roots are cut, the sensory afflux is removed and the spasticity becomes diminished or disappears entirely. A large number of operations have since been performed, and in a certain number of cases satisfactory results have been obtained. Spastic diplegia and hemiplegia can, therefore, sometimes derive a certain amount of benefit from **Förster's operation**. For the upper extremity the last four cervical roots, and for the lower extremity the last three or four lumbar, also the first and second sacral roots should be removed on both sides. Immediately following the operation the **limbs should be placed in removable plaster splints in corrected positions**. The splints should be kept on for a very long time and removed only for the exercises, which must be carried out several times a day. This **after-treatment** is very important and Förster insists upon careful exercises during a very long period after the operation.

Recently Schwab and Allison<sup>159</sup> devised a method of treatment of the spasticity and athetosis which they called "**muscle group isolation**." It consists of isolating muscles or groups of muscles which are at fault in production of contracture, deformity or athetosis. It is done by cutting off, from the central nervous system, the connection along which the abnormal impulse is transmitted. This is accomplished by isolating the nerve innervating the affected muscles and injecting it with alcohol. A paralysis of these muscles will thus be induced without interfering with the antagonistic muscles. The subsequent treatment will consist of massage and physiological exercises. In Little's disease, for example, the obturator nerve which supplies the adductor muscles of the thigh to

be injected with alcohol. This method is also advisable in deformities from anterior poliomyelitis.

Another method for "muscle isolation" in treatment of spastic paralysis was devised by Stoffel.<sup>160</sup> His operation aims to weaken the contracted muscle by depriving it of a certain part of its innervation, while at the same time the antagonist muscle is strengthened by massage and exercises. When the nerve is exposed for three or four centimeters, its different fibers are touched with a needle electrode carrying a current so weak that the innervated muscle barely twitches. It is thus possible to single out the nerve fibers involved. With this information the tract innervating the muscle involved in the contracture is worked loose for a distance of five or seven centimeters. The nerve bundle is then severed in case of severe contracture, or only part of the fibers. The aftertreatment is very important. When the operation is correctly performed and suitable aftercare with massage and exercise is given, there will be a certainty of success in correcting spastic contracture of any form and duration. Stoffel<sup>161</sup> gives a final review of his many cases, almost all ending successfully.

Sharp<sup>162</sup> found that in a large number of hemiplegies, paraplegies and diplegies there were signs of increased intracranial pressure. He considers it of great importance to relieve this increased pressure as a means of lessening the spasticity and improving the mental condition. He formulates his views in the following manner: Cases with definite histories of difficult labor (with or without instruments), in which signs of intracranial pressure are shown in dilated retinal veins, haziness of optic disks, especially in the nasal halves, in high tension of cerebrospinal fluid at lumbar puncture, should undergo a subtemporal decompression on the right side. If pressure remains high a left subtemporal decompression is performed the following week. The pathological lesions found are treated according to the findings. The latter are removed, punctured if a cyst, or the outer wall of the latter excised. The after-treatment consists of the routine orthopedic measures, viz., tenotomies, stretching of contracted muscles, braces, etc.

#### D. LETHARGIC ENCEPHALITIS

Recently attention has been called to a special cerebromeningeal syndrome, to which the name "lethargic encephalitis" is given.

**Symptoms.**—The condition, most frequently febrile, commences with pain in the head and sometimes with vomiting. Very rapidly somnolence sets in, which progressively becomes more and more marked. At first there is only a slight drowsiness, later a genuine sleep, from which, however, the patient can be aroused, but into which he soon falls again. In a more advanced stage the sleep resembles coma. The sleep may be interrupted by delirium, tremor and, exceptionally, by convulsions. Ordinarily there is only sleep.

The muscular apparatus of the eyes is almost invariably involved.

Paralysis of the levator palpebrarum, nystagmus and, more rarely, diplopia are observed.

**Diagnosis.**—From the diagnostic standpoint meningitis is naturally thought of either as a serous, a cerebrospinal, or else a tuberculous meningitis. But the ordinary signs of meningitis are either slightly marked or entirely absent. It is true that pressure on the ocular globes, as observed in these cases, is painful (a sign characteristic of meningitis), nevertheless, irregularity of the pulse and respiration (also characteristic of meningitis) are here wanting. Rigidity of the neck and Kernig's sign are either slight or totally absent. The cerebrospinal fluid is clear, contains a normal quantity of albumin and only two or three cells—rarely more than seven cells. Cultures fail to reveal bacteria.

**Prognosis.**—Out of seven patients recently observed by Netter,<sup>163</sup> two died—one in several hours, the other in eleven days. One recovered in several days and the remaining are still living, but their condition is very precarious.

In 1889-1890 in the course of an epidemic of influenza in Italy, Bulgaria, Denmark and in Germany a similar state of prolonged insomnia occurred and fatal results were frequently observed. Von Economo<sup>164</sup> observed a similar condition in Vienna which he also named encephalitis lethargica.

**Pathology.**—Pathologically, microscopical lesions are found in the cortex, pons, medulla and especially in the basal ganglia. They are: cellular infiltration of the blood-vessels with predominance in the gray matter of the third ventricle, in the region of the oculomotor nuclei around the aqueduct of Sylvius; the cells are altered. The analogy with the lesions of poliomyelitis is evident, but the spinal cord is intact. Von Wiesner<sup>165</sup> produced experimentally the lesion of encephalitis lethargica. He inoculated the brain substance under the dura of a monkey and thus induced a lethargic state. Autopsy showed a hemorrhagic encephalitis without lesions of the spinal cord.

## CONCUSSION OF THE BRAIN

### (*Commotio Cerebri*)

The common belief, that only in injuries accompanied by loss of consciousness is there concussion of the brain, is erroneous. In concussion there may be either complete unconsciousness or only vertigo, or a transient mental hebetude, or else such a mental state that the recollection of the accident is hazy. In all such cases symptoms of a grave nature may develop immediately or some time after the accident. Appreciation of the milder forms of cerebral concussion is of practical importance, for, if they are overlooked, serious consequences may follow.

The **pathogenesis** of concussion is still debatable. The following views are held:

(1) There is no material lesion in the nervous system and the disturbances are purely dynamic or else they are due to some perturbation in the cerebral circulation.

(2) There are some material lesions; they may be seen either macroscopically or microscopically in the medulla, and affect particularly the cardiac and respiratory centers.

(3) The cause of death lies in anemia of the respiratory center. The anemia is the result of a compression of the blood-vessels produced by edema of the brain. The edema is caused by a paralytic vasodilatation brought on by the trauma.

**Etiology.**—Concussion or jarring of the brain is always present in gross injuries of the cerebral tissue. But it may also occur without brain injury, either from a direct trauma of the skull—such as a fall on the head or a blow, or from an indirect injury—such as striking any other part of the body during a sudden fall, landing suddenly on the feet, falling on the buttocks, etc. In the present study we will be concerned exclusively with concussion without gross cerebral lesions.

**Symptoms.**—In the *severe cases* with unconsciousness, after the patient regains consciousness he will present, for some time, a mental hebetude which will be noticeable from the vague expression of his face. He will complain of headache, especially in the occipital region, also of tinnitus aurium. Insomnia, apathy and irritability are present. Mental dullness with an inability of concentrating his thoughts will be conspicuous. There is exhaustion upon the least exertion. On the slightest attempt to do anything, he will be covered with perspiration. The pulse is characteristic in that it is easily compressible and increases in rapidity while the patient is under examination. Temporary glycosuria has been observed by some writers.

In *mild cases* without much or any disturbance of consciousness the immediate effect of concussion will be pain in the head, some dizziness, vomiting at times, and general weakness. The pulse presents the same peculiarity as in the severe cases. Insomnia, restlessness, photophobia, loss of appetite, and constipation are present.

Weber and Neubert<sup>166</sup> observed an inability to do any muscular work. The distribution of the blood during muscular exertion differs from the distribution under normal conditions. The concussion injures the central mechanism for the innervation of the blood-vessels. Both the peripheral and cerebral blood-vessels are involved. It is therefore evident that this is the cause of the headache and of other symptoms which follow and persist after concussion of the brain. The headache and dizziness are connected with the damaged central mechanism for the innervation of the vessels, as also the weakness and inability to do muscular work. The latter finds its explanation in this curious fact that the vessels shrink instead of becoming distended during muscular exertion.

**Prognosis.**—The prognosis is variable. Even in the severest form recovery may follow. On the other hand mild cases may last months

and years and recovery may remain incomplete. In the majority of cases, especially when there are no complications, such as fracture of the skull, when there is no history of syphilis or alcoholism, also when the treatment is instituted at the earliest possible moment, recovery may be complete.

An incomplete recovery consists of a continuous asthenic condition, loss of weight, pains in the head and change of disposition. Irritability and difficulty of adapting oneself to surroundings may remain for years. In a certain group of cases mental symptoms of a graver nature may develop. The following disturbances have been observed: Transitory or permanent defects of intelligence, especially of memory, such as inability to retain impressions and retrograde amnesia; delirium, which may be associated with profound mental alterations ending in dementia; hallucinosis, Korsakoff's psychosis, even in individuals free from alcoholism; finally dementia may be the ultimate outcome of concussion of the brain. In children, when concussion occurs at an early age, arrest of mental development may result.

**Treatment.**—The most essential principle of treatment is **absolute rest in bed**, and this must be instituted **as early as possible** after the injury. This applies to the severe as well as to the mildest cases. The various manifestations should be treated symptomatically. **Sedatives, purgatives, light diet, avoidance of stimulation of excitement and of noise**, are all that is necessary. Confinement in bed must be as long as possible. Neglect of recognizing the importance of early treatment may render the patients permanent invalids.

Weber and Neubert (*loc. cit.*) obtained surprising benefit from alternating hot and cold douches. At first the relief is transient, but the improvement becomes permanent under a course of alternating douches. The relief is striking within half an hour even after one alternating douche, and in two or three weeks the improvement becomes a complete cure. The douches are given with hot and cold water for half a minute each (54° and 113° F.), applying the cold jet a little longer than the hot, and ending always with cold. The cold seems to be the active factor; its effect is merely enhanced by the hot jet.

## NERVOUS DISORDERS FOLLOWING VIOLENT EXPLOSIONS

In the section on Meningeal Hemorrhages some consideration was given to this subject. In the present section all possible nervous disturbances will be described, such as were seen and studied in the war by various observers.

The history given by the patients themselves is always the same: projection of the body in the air, fall, and very frequently loss of consciousness of greater or less duration. It seems that the explosion alone is not sufficient; there are almost always some additional elements which favor the development of the nervous disturbances. Some patients, for example, claim that the shock caused by the explosion was particularly

controllable and the effect of it was very brief. Fatigue and depression usually resulting from continuous bombardment, apparently predispose to nervous disturbances.

**Varieties of Disorders.**—As to the varieties of nervous manifestations, they are manifold. Generally speaking, the observations reported by the British, French and German observers can be divided into three groups, viz., *nervous*, *mental* and *neuropsychotic* disturbances. Tremors, convulsive seizures, hemiplegia, paraplegia, monoplegia, disturbances of micturition and defecation, choreic phenomena, headache, neurasthenia—these are the symptoms of the first group. To the second group belong: mental confusion, delirium, stupor and amnesia. In the third group are found individuals with mental confusion, with psychasthenia and hysteria and at the same time presenting disturbances in the neurosensory apparatus or in the domain of a special sensorium, such as deafness and speech defect, or mutism or aphonia.

In view of the absence of external injuries, the question naturally arose in the minds of the observers on the battlefield as to whether the manifestations mentioned were of an organic or of a functional character. In the vast material already accumulated there are cases with undoubted signs of involvement of the central nervous system, from the standpoint of reflexes and the state of cerebrospinal fluid—cases which are not amenable to treatment with psychotherapy. In some of these cases a careful analysis revealed the presence of a traumatism to the spine during the phase of falling, after the violent explosions. In other cases cerebral symptoms followed explosions and the patients died shortly afterward. Autopsies revealed hemorrhages in the meninges of the brain and in the cord (*see* section on Meningeal Hemorrhages). Finally there are cases in which tremors, paraplegia, hemiplegia and astasia-abasia have been observed, and they all proved to be of a functional character, in view of the absence of typical changes in the reflexes and because of their recovery after an appropriate psychotherapeutic treatment.

**Pathogenesis.**—As to the pathogenesis in the cases with evidences of organic lesions of the central nervous system, it was discussed in the section on Meningeal Hemorrhages. It was pointed out that the analogy with what occurs in caisson disease in regard to the effect of abrupt decompression is great, namely the production of gaseous embolisms caused by sudden withdrawal of gas from the blood in which the latter accumulated in excess during the phase of compression.

The phenomena observed could be explained also on the basis of sudden vascular distention in the viscera produced by considerable external pressure. The increase of blood-pressure is particularly seen in the brain and spinal cord, and the blood-vessels of the latter are apt to rupture. The vascular distention readily explains the cerebral congestion which sometimes persist for weeks and months and causes paralytic phenomena in some cases. It may explain also the inequality of pupils and vaso-motor disturbances, both sympathetic phenomena observed in cases of emotion. It is therefore evident that while there are cases of hysteromatism, such as are observed in civil life in neuropathic indi-



viduals, there are also cases of undoubted organic origin. Commotion is not emotion, neuropaths are not the only victims, and apart from the emotional phenomena which accompany it, it has in some cases an origin, evolution and consequences of an organic character.

**Prognosis.**—The prognosis varies with the nature and intensity of the manifestations. The experience of various observers shows that if some phenomena—such as tremors, speech disturbances, auditory disturbances, torticollis, paralysis—all recover promptly if treated very early, there are others which last a considerable time. To the latter belong the mental phenomena, such as confusion and psychasthenic symptoms which require isolation and prolonged rest. It must be also borne in mind that traumatism of this character usually develops an abnormal emotionality which is a strong predisposing factor to repetitions of the disorder whenever new emotional accidents occur.

The reader is referred also to the section on Meningeal Hemorrhage in Commotions.

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## CHAPTER V

### APOPLEXY

#### *(Hemorrhage—Embolism—Thrombosis)*

By ALFRED GORDON, M.A., M.D., F.A.C.P.

Hemorrhage, p. 555—Softening of the brain (embolism and thrombosis), p. 558—Hemiplegia, p. 561—Prognosis of apoplexy and evolution of hemiplegia, p. 570—Diagnosis of apoplexy and hemiplegia, p. 571—Diagnosis of the pre-apoplectic period, p. 571—Diagnosis of the apoplectic attack, p. 572—Diagnosis of hysterical hemiplegia, p. 574—Diagnosis of hemiplegia according to the localization of the lesion, p. 574—Monoplegia, p. 576—Treatment of apoplexy and hemiplegia, p. 577—Syphilitic hemiplegia, p. 580—Ingravescent or progressive apoplexy, p. 580—Delayed apoplexy, p. 580—Homo-lateral hemiplegia, p. 581—Intermittent closing of cerebral arteries and transitory hemiplegia, p. 582—Cerebral arteriosclerosis, p. 583—Meningeal hemorrhage, p. 584—Cerebro-subarachnoid hemorrhage, p. 584—Meningocerebral hemorrhage, p. 584—Hemorrhagic meningo-encephalitis in young individuals, p. 584—Meningeal hemorrhage due to trauma, p. 586—Meningeal hemorrhage following explosions, but without external injury, p. 587—Pachymeningitis hemorrhagica interna, p. 589—Meningeal hemorrhage in the newly born, p. 590—Thrombosis of the intracranial sinuses, p. 593.

Apoplexy is characterized by a sudden loss of consciousness followed by a complete or partial loss of power (and sometimes of sensations) on one side of the body. (In some cases consciousness is preserved.) The most common immediate causes are: hemorrhage, embolism and thrombosis. The three conditions lead to one final result, namely, hemiplegia, but the pathological lesions and the course of the disease are not identical.

### A. HEMORRHAGE

**Pathology.**—Rupture of a blood-vessel and a flow of blood into the brain is the essential condition. The most frequent seat of cerebral hemorrhage is the internal capsule and the surrounding basal ganglia. The reason of this predilection lies in the fact that the arteries distributed to these parts, namely, the lenticulostriate and lenticulothalamic arteries, are small, fragile, arise directly from large and strong vessels without the usual graduated transition in size, do not anastomose among themselves or with other vessels, and have no collaterals. All these circumstances render them more apt to rupture, when under high pressure, than the cortical vessels, for example, which branch a great deal.

Durant-Fardel has shown that these same arteries frequently develop miliary aneurysms which are caused by degeneration of vessel wall (peri- and endarteritis).

Hemorrhages in the neighborhood of the ventricles may break into the ventricles. Rupture of blood-vessels on the convexity or at the base of the brain is rare. The clot which forms after a hemorrhage and the



FIG. 1.—HEMORRHAGE IN THE INTERNAL CAPSULE.  
(Gordon, *Archives of Internal Medicine*.)

adjacent brain tissue undergo certain changes. The red color of the clot gradually changes into yellow. The serum is pressed out and removed by the blood and lymph. Leukocytes absorb the red blood corpuscles. The nervous tissue which is affected by the clot is liquefied and eventually absorbed. The neighboring tissue being compressed, suffers in its turn; the connective tissue and neuroglia proliferate and form a thick capsule around the softened focus, and a cyst containing a yellowish fluid is the result. When the contents of the cyst are absorbed, its walls shrink and a cicatrix is formed. Frequently the con-

of events is not so favorable: the ruptured artery continues to ooze, the destruction of the brain tissue continues and various structures of the brain are under considerable pressure.

When a hemorrhage occurs on the surface of the brain, beneath or within the membranes, the clot may not become organized and destruction of cortical tissue may thus be avoided, so that the brain will resume its function when the clot is removed.

In the brains from aged individuals Ferrand observed a special state of cerebral tissue characterized by small cavities (*lacunes*), in the center of which was seen an artery. These cavities are due to a disintegration of the nervous elements. As the blood pressure is invariably increased in advanced age, the atheromatous central artery is easily ruptured when the blood-vessel is under high tension.

The most important consequence of cerebral hemorrhage is its effect on the nervous tissue beneath and in the immediate vicinity of the area destroyed by the clot. Secondary degeneration is the usual result. It may be traced through an entire tract. A hemorrhage, for example, in the posterior limb of the internal capsule will be followed by a descending degeneration in the entire motor pathway, even in the lowest portion of the cord. The degeneration is characterized at first by disappearance of the myelin and nerve-fibers, which are ultimately replaced by connective tissue and a scar is thus formed.

**Etiology.**—A degenerative state of the vascular walls is the chief underlying cause of non-traumatic cerebral hemorrhages. In such cases increased blood-pressure will readily rupture the altered vessel wall. This occurs in severe muscular efforts, as, for example, in lifting heavy weights, in the act of difficult defecation, in parturition, in paroxysms of severe cough, coitus, attacks of anger, excitement, indulgence in spirituous liquors, etc.

As to the causes of alteration of the walls of the blood-vessels, it occurs mostly in the degenerative period of life, and in the majority of cases cerebral hemorrhage takes place after forty years of age. Vascular changes are observed in arteriosclerosis, syphilis and lead intoxication. Alcohol also predisposes to an atheromatous state of the blood-vessels. Pernicious anemia, purpura, scurvy, chronic nephritis, finally aortic insufficiency by its constant fluctuation in blood-pressure—all lead to degenerative conditions of the blood-vessels.

Men are more liable to cerebral hemorrhage than women. Sometimes a hereditary predisposition is observed: some families suffer for several generations from apoplexy. It is possible that in such cases hereditary syphilis produced a poor wearing quality of the blood-vessels.

Irrespective of arterial alterations, cerebral hemorrhage may occur from traumatic causes, such as fracture of the skull, blows or contusion. Hemorrhages on the surface of the brain are usually the result of direct cranial traumata, although they may also occur under the conditions related above.

**Symptoms.**—An attack of apoplexy may come on suddenly or gradually and is usually preceded by some precursory symptoms, such as:



plished either by a clot or a particle of fibrin carried from diseased valves of the heart, or else by a fragment of an atheromatous plaque. The clot usually degenerates and sometimes becomes calcified. The obstructed blood-vessel may become a fibrous cord. As some cases of embolism recover, it is probable that the collateral circulation assists in keeping up the nutrition of the area supplied by the obstructed blood vessel. In thrombosis, recovery cannot take place because the diseased artery is surrounded by other atheromatous vessels and collateral circulation is of no special usefulness.

The most frequent seat of cerebral softening is in the zone of the basal ganglia. The left hemisphere is more frequently affected by embolism than the right. The middle cerebral arteries and their branches are the usual seat for embolism and the basal arteries for thrombosis.

**Etiology.**—**EMBOLISM.**—It is of cardiac origin. Emboli arise mostly from the left side of the heart in endocarditis, although they may come from other sources, from the lungs, for example. Vegetations on the mitral valve or clots may be detached in a physical effort, in a shock or a severe cough, and thrown into the circulation; they thus reach the cerebral arteries and obstruct them. In ulcerative endocarditis the detached particles will carry microorganisms and produce, besides embolism, an inflammation of the surrounding tissue.

**THROMBOSIS.**—It is of arterial origin. An endarteritis narrows or obliterates the lumen of the blood-vessel, and coagulation of blood follows. Syphilis in young individuals, arteriosclerosis in advanced age, chronic intoxications, such as lead and alcohol, are the usual causes of formation of thrombus. In cases with a weak myocardium, which produces a retardation of circulation, such as observed in cachexia, infectious diseases, chlorosis, thrombosis may occur. Similar conditions are also seen in diabetes and gout, which favor the coagulation of blood and therefore produce thrombosis. In old individuals unusual exertion is apt to produce thrombosis; the latter commonly occurs in the night after fatigue.

**Symptoms.**—The attack of apoplexy is not as intense and enduring as in hemorrhage. The loss of consciousness, which is almost constant in hemorrhage, is frequently missing here. If the lumen of a large artery is occluded, sudden loss of consciousness will occur. In occlusions of small arteries with emboli and in thrombosis of arteries of any size there is usually no loss of consciousness. The onset may be sudden or gradual, although in embolism it is usually sudden. The coma is milder than in hemorrhage and the other symptoms which accompany coma are also different in both cases. In embolism the pulse is not retarded, the face is pale, the temperature rises immediately. When the onset is gradual, prodromal symptoms are always present. Twenty-four or forty-eight hours before the onset of the paralysis there is a sensation of numbness or slight pain in the extremities which are to become paralyzed. This is soon followed by a weakness, at first of the fingers or toes, which gradually progresses and involves the entire limb. The paretic condition becomes a genuine paralysis at the end of 24 h.

days. Sometimes collateral circulation intervenes and then amelioration of symptoms is seen instead of complete paralysis.

A gradual onset of apoplexy due to a gradual softening is, of course, met with in the progressive arterial degeneration of advanced age.

When the arterial obstruction occurs in the cortex, instead of coma, epileptiform convulsions will be present. The latter may be focal and confined to the limbs which will eventually become paralyzed, or else they may be generalized.

### *Hemiplegia*

As mentioned above, the final result of apoplectic seizures is the more or less complete loss of voluntary power in one-half of the body, viz., hemiplegia. Hemiplegia is total when the face is involved in addition to the arm and leg. The loss of power may be complete or incomplete. When one limb is affected, the condition is called monoplegia.

**Symptoms.**—Organic hemiplegia is always the result of a lesion, either of the cortical motor neurons or of the fibers coming from these neurons which constitute the pyramidal bundles. The latter may be affected at any level of the entire pathway from its place of origin (motor pyramidal cells in the cortex) down to the lower portion of the spinal cord. Organic hemiplegia, therefore, may be cerebral or spinal, the former by far the more frequent. In cerebral hemiplegia the paralysis is, in the majority of the cases, on the opposite side because of the decussation of the pyramidal tracts. In spinal hemiplegia the paralysis is on the side of the lesion. Two phases should be considered in the course of cerebral hemiplegia: one is that of flaccidity, the other that of rigidity with later contractures.

**A. FLACCID PHASE.**—At the onset, and a short time after the onset, the paralysis is flaccid. When the arm and leg are raised and abandoned, they fall as inert bodies; all movements are abolished. The cheek on the same side is raised at each expiratory movement. The cornea is anesthetic on the paralyzed side. The conjugate deviation of the head and eyes, when present, is towards the paralyzed side at the onset, but, as was mentioned in the preceding section, it soon changes to the opposite side and the patient will "look at the lesion." In complete hemiplegia the face is paralyzed, the angle of the mouth is drawn to the sound side, so that the angle of the mouth on the paralyzed side is at a lower level than that on the sound side. The paralyzed cheek is lowered, its wrinkles and the nasolabial fold on this side are smoothed out. The facial asymmetry is particularly evident when the patient speaks or laughs. He cannot blow or whistle. The tongue, when protruded, is deviated toward the paralyzed side. Beevor<sup>2</sup> explains this phenomenon by the fact that there are two cortical centers for the movement of the tongue, one in the upper part of the tongue area, which causes deflection toward the opposite side, and another situated lower and more anteriorly, stimulation of which causes protrusion of the tongue in the middle line. The latter affects equally the movements on

the two sides of the tongue, and it is the disturbance of this movement which causes the flexion of the tongue toward the hemiplegic side and not the voluntary movement of turning the tongue into the cheek on the paralyzed side. The tongue on the paralyzed side loses its elasticity



FIG. 3.—CASE OF RIGHT HEMIPLEGIA.

and is flabby. When lying in its gavity, the posterior part especially appears to be thickened and not as wide in comparison to the normal side. The uvula is deviated towards the sound side. In some cases of hemiplegia there is also weakness of the soft palate: at rest the palate appears to be flatter and broader than on the sound side; in phonation the palate is drawn upward and towards the normal side. This

observed by Tetzner<sup>3</sup> in 77 per cent. of cases of cerebral hemiplegia. Mastication, deglutition and phonation are always somewhat disturbed. The food accumulates in the mouth on the affected side and runs out partly on the same side, so that there is abundant salivation from the mouth. The general opinion is that only the lower portion of the facial nerve is involved in cerebral hemiplegia, but close observation will reveal that almost in every case the upper facial nerve is also affected but to a much lesser degree than the lower one. This relative integrity of the upper facial nerve may be due to the following possibilities: (1) different course of the fibers of the upper and lower portions of the facial nerve; (2) bilateral innervation of the orbicularis palpebrarum muscle (Broadbent). The muscles of the trunk are but very slightly involved. Beevor noticed a weakness of these muscles in a certain number of cases. The muscles of the neck, spine and abdomen are only very slightly involved because of innervation of their muscles by both hemispheres. Bilaterally associated movements are controlled by the motor cortex of both hemispheres. This can be seen from the inability to move voluntarily one side of the chest without moving the other, or one side of the forehead without the other.

In the upper and lower limbs voluntary motion has totally disappeared. The arm lies close to the trunk, the leg is extended when in bed. Their muscles are flaccid.

The muscles of the larynx are, as a rule, not involved because of the bilateral action of the cortical center.

The sphincters are slightly disturbed or not at all.

The reflexes are very frequently abolished in the beginning or else much diminished. However, not rarely Babinski's reflex is elicited at the onset of hemiplegia. The same may be said of the author's "paradoxical flexor reflex." It was found in some cases before Babinski's sign made its appearance. The reflex consists of extension of the great toe or of all the toes when the calf muscles of the leg are deeply pressed upon.<sup>4</sup>

This flaccid phase may last from several weeks to three months. The paralysis may disappear, but more frequently the second phase sets in. Ordinarily the lower limb commences to improve and the face largely recovers, but the arm, on the contrary, improves very slightly. As a rule, the paralysis is more marked in the distant than in the proximal portions of the limb.

Occasionally contractures may be observed in the first phase of hemiplegia; but this is of a grave outlook, as it indicates a hemorrhagic invasion of the ventricles. Sometimes early convulsions are observed, which are an indication of corticomeningeal lesion.

**B. PHASE OF CONTRACTURE.**—When the symptoms of paralysis do not disappear, the affected portions of the body gradually enter into a state of secondary contractures. Gradually the limbs become rigid and difficult to move. The rigidity continues to increase and becomes permanent. In exceptional cases and especially when the contracted

muscles undergo atrophic changes, the rigidity, instead of increasing, decreases.

When the muscles of the face become contracted (which is rare), the deviation of its features is in the opposite direction, viz., toward the paralyzed side.

The muscles of mastication, those of the trunk and of the larynx escape contracture.

Final contracture develops usually about three months after the apoplectic attack. Its course is slow but invariably progressive. Its appearance is indicated by the exaggeration of the tendon reflexes and the presence of ankle-clonus and toe-phenomenon. In some rare cases the contracture remains for a long time in a latent state and the only symptom is the increased tendon reflexes; but more frequently contracture progresses gradually, so that it finally becomes permanent. In the latter case deformities of the extremities are inevitable. They will be multiple according to whether the flexor or extensor groups of muscles are affected.

(a) *Flexor Type*.—In the flexor type the following condition is observed: the shoulder is raised, the arm is held close to the body in forced adduction with inward rotation, the elbow is flexed, the hand is flexed and in pronation, the fingers are flexed, especially in their second and third phalanges. In the lower extremity, the flexion type is rare and is seen only in hemiplegics who have been confined to bed for a long time.

(b) *Extension Type*.—The extension type is very rare in the upper extremity; but, on the contrary, is the rule in the lower extremity. The thigh and leg are on a straight line, the foot is in a position of equinovarus, less in cases of adult hemiplegia than in infantile hemiplegia, the toes are sometimes flexed.

As a rule, the paralysis and contracture is less marked in the lower than in the upper extremity. In spite of the contracture, the hemiplegic can walk. His gait is characteristic: he does not flex the knee or the ankle, all the movements are executed at the hip-joint; in carrying the limb forward he does it in the form of a circle because of inability of flexing the limb; the foot scrapes the floor. Patients with a marked equinovarus makes small steps, slowly placing the leg forward, and the foot scrapes the ground with its toes.

In the upper extremity there may be equal variations of position of its components. Thus there may be extreme flexion of the forearm over the arm and flexion of the hand and fingers. There may be a moderate flexion of the forearm and extreme flexion of the hand. Complete closure of the hand also occurs. The deformities described may be modified by passive movements, but the limbs easily return to the former positions. In cases of old standing, passive movements cannot make the least change, as here the position is fixed because of adhesions in the synovial membranes of the joints and because of retraction of the muscles.

(c) *Associated Movements*.—While the contracted limbs are in the

to execute any voluntary movements, nevertheless involuntary movements will be observed in them when passive or voluntary movements are produced by the limbs of the opposite side. They are called "associated movements" or "synkinesies" of the French writers. They may be brought in evidence by the following procedure: The patient is told to squeeze an object with his sound hand. Immediately the left hand will also close in the same manner. The amplitude of the latter movement is in proportion to the voluntary movement of the sound side. Not only the hand will close, but the flexed elbow will increase the flexion and the fingers will close more.

Associated movements may be observed on the sound side when the affected limbs attempt to execute movements. Babinski, in 1897, made a special study of associated movements which he has shown to be pathognomonic of organic hemiplegia; they are absent in functional paralysis. They are, therefore, of diagnostic importance. He observed the following phenomena: when in dorsal position, with arms crossed over the thorax, the patient attempts to sit up: on the paralyzed side the thigh flexes over the pelvis and the heel is raised, while on the sound side the limb remains immobile or else executes similar movements but of extremely slight degree and much delayed. The same is observed when, being seated, with the arms in the former position, he attempts to fall back. When the patient, in dorsal position with arms crossed over the thorax and legs hanging down over the foot of the bed, makes an effort to sit up: on the paralyzed side the thigh flexes over the pelvis and the leg extends over the thigh. This *combined flexion of the thigh and trunk* is a sign of diagnostic significance.

Grasset and Gaussel have observed that, when the paralysis is not pronounced, the patient is able to raise separately each leg off the bed, but cannot raise both legs simultaneously; also, when, in dorsal position, he raises his paralyzed leg, it falls heavily back at the moment the sound leg is elevated by another person.

Strümpell's *tibialis anticus muscle phenomenon* is another diagnostic sign of associated movements in organic hemiplegia. When the patient flexes the leg over the thigh, the contraction of the tibialis anticus is accompanied by dorsal flexion and adduction of the foot. This phenomenon is more evident when the movement of the leg is resisted by another person.

Hoover observed that when the patient attempts to raise the sound leg off the bed, the heel of the paralyzed leg presses energetically against the bed. This is called "*opposition movement*."

Rainiste observed that when, the patient being in dorsal position and his legs separated, he is told to move the sound leg to the paralyzed leg and at the same time the movement is opposed, the paralyzed leg will move toward the sound leg.

Néri described the following associated movement: When the patient, standing, leans forward, the paralyzed leg will flex at the knee: also when, in dorsal position, he raises alternately one leg at a time, the knee of the paralyzed leg flexes, but the sound leg remains straight.

In Souque's "*phénomène des doigts*," when the patient attempts to raise his paralyzed arm, the fingers spread out and remain separated from each other.

Marie and Foix's *retraction sign* consists of flexion of the thigh over the pelvis, of the leg over the thigh and of adduction of the foot when the toes are forced slowly downward.

(d) *Reflexes*.—After the flaccid period of hemiplegia commences to disappear and the spastic phase sets in, the following reflex phenomena make their appearance:

(1) *Lower Extremities*.—The tendon reflexes are exaggerated: the patellar tendon, the triceps and biceps reflexes are all increased in amplitude. When the patella is abruptly pushed downward, it is seized with ascending and descending movements for a few moments. This is the *patellar phenomenon* (trepidation). Ankle-clonus makes its appearance, also the toe-phenomenon of Babinski (1898) consisting of dorsal extension of the great toe or of all the toes with a fanlike separation of the latter when the sole of the paralyzed foot is stimulated.

Extension of the toes may be brought by Oppenheim's method when deep downward friction is exercised over the antero-external surface of the leg close to the tibia. Schäfer obtained the toe-phenomenon by pinching the tendo achillis, Gordon by deep pressure of the calf muscles, Throckmorton by percussing the base of the great toe, and Chadwick by scratching with a pin below the external malleolus.

Rossolimo observed flexion of the paralytic toes when their plantar surface is slightly percussed.

Mendel-Bechterew's sign consists of flexion of the four last toes upon percussion of the external aspect of the dorsum of the foot.

Hirschberg's sign consists of adduction with internal rotation of the foot upon friction of its inner border.

Néri's hypertonicity of flexors sign is elicited in the following manner: When, with the patient in a lying position, the paralyzed limb is raised by Lasègue's method to form an angle of 40-50 degrees, the leg flexes over the thigh.

Logre observed spontaneous extension of the great toe when the leg is given Lasègue's position or the position for elicitation of Kernig's sign.

Claude's reflex-hyperkinesia consists of voluntary movements of extension or retraction of a totally paralyzed limb when it is pinched or pricked or else deeply pressed upon. When the phenomenon is present, the prognosis is favorable.

(2) *Upper Extremities*.—For the upper extremities the following reflexes have been observed in organic hemiplegia:

The *sign of the thumb* (Klippel and Weil) consists of involuntary flexion of the thumb when an effort is made to extend slowly the four other fingers which are in a state of contracture.

*Exaggerated Flexion of the Forearm* (Babinski).—When the supinated forearm is elevated and flexed over the arm, the degree of

flexion is greater than in a normal arm when the movement is persisted in.

*Automatic Pronation Sign* (Babinski).—This is elicited as follows: The palmar surface of the patient's hands face each other and their thumbs are upward. In this position they are placed in the examiner's hands, which give them several jars and thus make them jump up and down. The sound hand remains in the vertical position, while the paralyzed hand falls in pronation with the palm downward.

*Pronation Phenomenon* (Strümpell).—When the forearm is flexed over the arm, the former places itself in pronation so that the hand approaches the shoulder not by its palmar, but by its dorsal surface. It is observed even in mild contractures.

*Bechterew's sign* is elicited as follows: When both forearms, after having been flexed over the arms, are relaxed, the hemiplegic forearm will fall back more slowly and in two periods, even when the contracture is mild.

*Rainiste's Sign*.—The elbow of the paralyzed arm is on a table. The forearm and hand are both raised and kept in a vertical position by the observer's hand. The latter is gently removed from the patient's hand and slides down on the forearm; the paralyzed hand at once falls and forms with the forearm an angle of 130 degrees. This sign can be detected immediately after an apoplectic attack and during coma.

*The finger phenomenon* (Gordon's) consists of extension of all the fingers, or of the thumb and index when pressure is produced by the observer's thumb against the pisiform body. The sign is particularly prompt in recent hemiplegias.

*The wrist sign* (Chaddock) consists of flexion of the wrist and simultaneous extension and separation of all the fingers when scratching with a pointed instrument is done on the ulnar side at the junction of the palm and wrist.

(3) *The Face*.—For the face the following phenomena have been described:

During the comatose state there are anesthesia of the cornea and loss of the corneal reflex.

*Reverillod's sign* consists of an impossibility of voluntary isolated closure of the eye on the paralyzed side.

*McCarthy's sign* is an exaggerated supra-orbital reflex which is elicited by percussion of the supra-orbital nerve: the contraction of the orbicularis is pronounced.

*Babinski's Platysma Sign*.—When the patient flexes the chin against the chest or else opens his mouth and these movements are opposed, a contraction of the platysma myoides is observed on the sound side, but not on the hemiplegic side.

**Complications.**—A. SENSORY DISTURBANCES.—Paresthesias (numbness, tingling, etc.) are not infrequent in the prehemiplegic state. They sometimes announce, so to speak, the oncoming paralysis. They are localized on the side which is to be paralyzed.

In the majority of cases objective sensory disturbances are present



on the hemiplegic side. Sometimes the loss of sensations is absolute or in proportion with the loss of motor power. In some cases the sensory disturbances are only transitory and most of the time they develop shortly after the onset of hemiplegia. The characteristic feature of sensory disturbances of cerebral origin (cortical or capsular) is their disturbance in the distal end of the limbs. To avoid repetition, the reader is referred to the section on Sensory Disturbances of Cerebral Origin, in which the subject is discussed in details.

**B. MOTOR DISTURBANCES.**—Similar to sensory phenomena, some motor disturbances may also occur in the prehemiplegic state. Some involuntary movements, choreiform or others of very short duration, also localized epileptiform convulsions, may appear before the hemiplegia sets in.

*Hemichorea*, *hemiathetosis*, *hemiataxia* and *dysmetria* sometimes accompany hemiplegia. *Tremor* resembling that of paralysis agitans (Charcot) or that of multiple sclerosis (Raymond) has been observed. In some cases there may be a combination of both, passive and intention tremor.

*Hemichorea* usually appears after the first phase of the hemiplegia. It is in evidence when the affected limb is at rest and increases upon voluntary movements. The face is, as a rule, not involved. Hemichorea is frequently accompanied by hemianesthesia.

*Hemiathetosis* is confined to the hand and foot of the paralyzed side. It consists of slow and exaggerated involuntary movements of flexion and extension, abduction and adduction of the fingers, toes, wrist and ankle. The movements are continuous but increased upon voluntary efforts and upon emotion. They disappear during sleep. Sometimes temporary contractures occur in the affected fingers or toes, so that the hand or foot is placed in a forced and fixed position for a short while.

In some cases hemiathetosis may be associated with hemichorea, the former being confined to the hand, and the latter to the upper part of the arm. Hemiathetosis is observed frequently in infantile cerebral hemiplegia, but rarely in adult hemiplegia.

The pathogenesis of the choreo-athetotic movements is a matter of dispute. The internal capsule (Charcot, Raymond), the posterior portion of the thalamus (Gowers and others), the pyramidal tract (Kahler, Pick), the lenticular and caudate nuclei (Vogt, Oppenheim)—have all been considered in the causation of the movements.

*Hemiataxia* consists of a disturbance of coördination in voluntary movements: the direction and precision of the movements are altered. The disorder is particularly marked when the patient closes his eyes. Since almost in every case of posthemiplegic hemiataxia there are sensory disturbances (superficial and deep), the ataxia finds its explanation. In all cases of cerebral hemianesthesia ataxia is present.

*Dysmetria*.—In cases of slight hemiplegia André-Thomas observed an inability to reach accurately an object with the hemiplegic limb; the latter oversteps the point of destination, as, for example, in the case

to nose movement. In cerebellar disease dysmetria is also present, but the movement is abrupt and rapid, while in hemiplegia it is slow.

C. VASOMOTOR AND TROPHIC DISTURBANCES.—Trophic disturbances in children will be discussed in the section on Cerebral Infantile Hemiplegia.

In adults the following complications have been observed:

Edema, desquamation and pigmentation of the skin, ulcerations, disturbed nutrition of the nails on the paralyzed side are not infrequent occurrences. Glossy skin of the hand is not rare. Bed-sores are quite frequent; they develop mainly at the points of contact of the skin with the bed. If the patient continues to remain in bed, the ulcerations of the skin may grow deeper, become gangrenous and produce a general infection and cause death.

Among the very frequent trophic disturbances is *muscular atrophy* on the paralyzed side. It may appear shortly after the apoplectic attack, or later. As an early occurrence it progresses rapidly. As a later occurrence it develops slowly. In the majority of cases it commences in the small muscles of the hand. In some cases the onset is in the scapular region (deltoid, supra- and infraspinatus muscles). The trunk is rarely involved. In the lower extremity atrophy is more rarely observed than in the upper. If it does occur, the antero-external group of muscles is principally affected. Deformities, such as claw-like hand, are the consequence of atrophy of the hand muscles. Reactions of degeneration are, as a rule, absent.

The pathogenesis of the muscular atrophy is not completely established. Lesions of the cells of the anterior cornua of the cord (Charcot, Leyden, Brissaud), peripheral neuritis (Dejerine), have been found at autopsies. Gille de la Tourette believes that the atrophy is due to the accompanying arthritis, but the latter is not present in every case. A cortical origin of the atrophy has also been considered.

*Arthropathies*.—They are observed mostly in the upper extremity: in the shoulder, fingers, elbow; they may be also in the knee and foot. They appear usually early, on about the fifteenth day after the apoplectic attack. The joint is red, edematous and very painful; its temperature is elevated. Synovitis with abundant seropurulent fluid, an inflammatory state of the sheaths of the tendons have been found at autopsies. The pathogenesis of the condition is probably dependent on the original cerebral lesion (Charcot, Brown-Séquard).

1). DISTURBANCE OF SPEECH.—*Motor aphasia* is a frequent accompaniment of the hemiplegia, *sensory aphasia* is rare. Sometimes there is only *anarthria* or *dysarthria*. (See section on Aphasia.)

*Impairment of intelligence* is not infrequent, especially in aged individuals. In left-sided hemiplegias the intelligence is usually preserved. *Memory* is frequently weakened. Change of disposition, of character, is quite common.

*Anosognosia*.—Babinski<sup>5</sup> called attention to a special psychic disorder which he observed in some cases. It consists of a modification of personal conscience to which he gave the name "*Anosognosia*." The

patient ignores or appears to ignore the existence of his paralysis. Such a patient is not confused or demented, he merely has no knowledge of his hemiplegia. In the cases which he studied, Babinski noticed that the patients were totally indifferent as to their affliction: they never complained of their helplessness, and when asked to move the paralyzed limbs they remained immovable as if the request did not concern them directly. It must be mentioned that in those cases there were also marked disturbances of sensations in the paralyzed limb and in one of them passive movements of the upper limb were not perceived. It is probable that the sensory disorder plays a predominant part in the genesis of anosognosia in hemiplegies.

### PROGNOSIS OF APOPLEXY AND EVOLUTION OF HEMIPLEGIA

During the apoplectic attack it is almost impossible to tell with exactness whether the patient will recover or not. If the coma is prolonged above twenty-four or forty-eight hours, the outlook is grave. It is equally bad when the bodily temperature goes down or ascends rapidly. It is also serious when the high temperature is continuous. A cardiac or valvular disease also renders the prognosis uncertain, as repetitions of apoplectic attacks are to be feared. Convulsions and early contractures are an indication of a profuse hemorrhage in the ventricles or in the meninges. Cheyne-Stokes respiration is a grave omen. Bed-sores are also an unfavorable sign. The presence of blood in the cerebrospinal fluid is a warning of impending danger, even if the clinical picture is at first mild. When the patient recovers from the coma, the question is to determine the future of the paralytic symptoms. An incomplete hemiplegia presents a favorable prognosis. However, if the paralysis is at first slight but during the following weeks becomes more pronounced, the chances for regaining the power in the affected limbs are slight. Appearance of contractures makes the prognosis serious. Hemiplegia due to traumatism or syphilis presents the best prognosis, as it is amenable to treatment. Complications (see above) make the prognosis unfavorable. Complete recovery is observed in only very small hemorrhages or in slight embolisms, provided a collateral circulation is promptly formed. Charcot claims that recovery, i.e., restoration of function, is possible only when the hemorrhage occurs in the corpus striatum, but no restoration is to be expected when the internal capsule is destroyed.

In the *second phase* of hemiplegia the contractures may be of great intensity: all movements are abolished, the joints are immobilized and the patient is bedridden. On the other hand, the contractures may be very slight. All possible intermediary degrees between these two extremes may be encountered. In the majority of cases the contracture is slight at first, but it progresses gradually to a certain degree and remains stationary. Exceptionally it retrogresses, so that the limbs may

present even a certain amount of flaccidity with loss of reflexes. In such cases there is usually pronounced muscular atrophy.

In some cases of apoplexy, instead of hemiparalysis, there may be only a hemiparesis, so that at first glance the weakness of the limb may be overlooked. In fact, there may be only a slight disturbance in gait or in handling objects or in executing fine acts, such as sewing, writing, buttoning, etc.

In some cases there may be contractures at the onset: They occur either in ventricular hemorrhages (*see* p. 563) or in cortical lesions. In the latter case the lesion is meningo-encephalitic (syphilis or tumor), the paralytic symptoms are slight or absent and the entire clinical picture consists of a contracture of the limbs which not infrequently are seized with localized epileptic convulsions. In such cases there is an irritation but not destruction of cerebral tissue. Removal of the irritating lesion by surgical intervention may give excellent results.

## DIAGNOSIS OF APOPLEXY AND HEMIPLEGIA

The discussion of diagnosis must embrace several important elements and phases. First of all the (*a*) *apoplexy*, next the (*b*) *hemiplegia*.

I. **Diagnosis of the Apoplexy.**—In apoplexy two phases must be considered: (1) the pre-apoplectic period and (2) the apoplectic attack itself. In the second part of the subject, not only the clinical diagnosis of hemiplegia is to be made, but also the localization of the lesion.

A. **DIAGNOSIS OF THE PRE-APOPLECTIC PERIOD.**—This is one of the most important chapters in the study of apoplexy, because it concerns conditions which, if recognized early enough, may serve as a therapeutic guide in preventing eventual apoplectic attacks.

In the sections on Pathology and Etiology, sufficient emphasis was laid on the degenerative state of the *arterial system* as being the chief factor in the causation of apoplexy from cerebral hemorrhage or thrombosis. Arterial degeneration is a slow process which requires years for its development. It is precisely the progressive changes that take place in the vessel wall with their effect on the brain, heart and kidney that constitute the most important prodromal period in apoplexy. Recognition, i.e., diagnosis of this period, is of practical value. The clinical picture is as follows:

Enlargement of the area of dullness over the heart and signs of cerebral arteriosclerosis, also sclerosis of the vessels of the kidney, are all signs suggesting impending cerebral hemorrhage in individuals inclined to obesity and past fifty years of age, especially when associated with persistent constipation. Long before the arteries feel hard or show a tortuous course, a permanent high blood-pressure reveals a tendency to arteriosclerosis with resultant overwork on the part of the heart. Löwenfeld, for example, found cardiac hypertrophy in 27 out of 40 cases, Kirk in 17 of 22, Kish in 5 of 13 cases. The manifestations of arteriosclerosis of capillaries in the brain are: frequent headache,

frequent transient vertigo, persistent disturbed sleep, forgetfulness, especially of names and figures, slight motor or sensory disturbances in the hand or foot, paresthesias in one arm or leg, sensations of heat in the head, change of disposition and mood. The presence of albumin in the urine reveals arteriosclerosis of the kidneys (especially in the obese); changes in the latter are found at autopsy, such as parenchymatous degeneration, granular atrophy, and hyperemia. Monakow found kidney disease in 30 per cent. of his apoplexy cases. Constipation and hemorrhoids, meteorism, feeling of oppression, dyspnea, are the visceral disturbances found in this category of individuals. Hereditary influences are also in evidence here. Not infrequently one observes apoplectic attacks occurring in several members of the same family and at about the same age.

This is the clinical picture of candidates for apoplexy. They are always predisposed to cerebral hemorrhages, and under the influence of factors, which are apt to upset the physiological or psychological equilibrium, apoplexy takes place. The factors which bring on the catastrophe are overexertion, overeating, straining at stool, violent emotions, such as sudden joy, etc.

**B. DIAGNOSIS OF THE ATTACK.**—Sudden loss of consciousness of cerebral origin does not always signify apoplexy. Generally speaking, there is no difficulty in diagnosing an apoplectic seizure. In exceptional cases it may be confounded with uremic and diabetic coma, syncope, intoxications (chloroform, alcohol, lead, etc.), and hysterical paroxysms, also hemorrhagic meningitis.

In *uremia* the onset of coma is slow and preceded by vomiting, dyspnea, convulsions and sometimes visual disturbances.

In *diabetic coma* there is difficult and deep breathing, followed by abrupt expiration, vomiting, diarrhea; the breath has the odor of chloroform and sugar is found in the urine.

In *syncope* consciousness is generally not totally lost; the pulse is small, irregular, respiration is unequal, face is pale.

*Intoxications*, such as alcohol and chloroform, will be recognized by the odor of the breath and the history of antecedents.

*Meningitis* may lead to coma and sometimes to hemiparesis, but it is accompanied by the characteristic generalized hyperesthesia. It leads to convulsions and contractures, to paralysis of the eye muscles and is accompanied by fever. Hemorrhagic meningitis accompanied by coma will be distinguished from apoplectic coma by the presence of convulsions, by absence of focal symptoms and rapid fatal termination.

Lumbar puncture will assist in determining the etiology of coma. In cases of meningeal involvement lymphocytosis is found; in diabetic coma acetone, in uremic coma excess of urea, in lead intoxication high pressure of cerebrospinal fluid.

*Hysterical paroxysm* may simulate an apoplectic attack, but the facial expression showing emotion, the preservation of the corneal reflexes, and the facility with which the intensity of the coma is modified, the normal

pulse and respiration, also normal color of the face will all enable one to recognize a hysterical attack.

After the diagnosis of apoplexy is established, it is necessary to determine whether the cause of it is hemorrhage or softening.

In favor of *hemorrhage*: There is usually absence of premonitory symptoms, its occurrence at advanced age, low temperature, profound and prolonged coma, completeness of paralysis, redness of the face, high tension of pulse and strong heart beats. A rapid and progressive improvement soon after the onset is also characteristic of hemorrhage.

The blood serum in cerebral hemorrhage presents a special diagnostic feature to which Marie and Léri<sup>o</sup> called attention. They observed a special greenish color which is probably due to the passage into the circulating blood of products of decomposition of hemoglobin in the hemorrhagic focus. To demonstrate this coloring, 10 to 20 c.c. of blood is collected in a tube; the serum is separated from the clot by any procedure. The greenish color is then observed. This simple method, called *chromo-serodiagnosis*, which does not necessitate special apparatus, is highly practical because it gives positive results in the first hours after the hemorrhage and persists for several days. It renders some assistance in the differential diagnosis between cerebral hemorrhage and softening or any other cerebral lesion.

In favor of *softening*: There is usually a rise of temperature, absence of coma or there is a mild and not prolonged coma, incompleteness of hemiplegia (usually a monoplegia), finally the presence of cardiac or arterial lesions.

Convulsions at the onset are more frequent in softening than in hemorrhage, especially if they are unilateral and when the lesion is cortical. Early convulsions and early contractures are indicative of a hemorrhage in the ventricles or in the meninges. Aphasia, if it occurs with a mild hemiplegia, is almost always due to a softening. Persistent aphasia is caused by softening. Hemianopsia suggests softening. Repetition of apoplectic attacks occurs in softening.

Lumbar puncture may render some assistance in the differentiation: In hemorrhage the effused blood passes into the cerebrospinal fluid (especially in ventricular hemorrhages) and will thus be detected, while in softening the spinal fluid remains clear.

The next step is to determine whether the softening is due to *embolism or thrombosis*: A sudden onset without premonitory symptoms in youth and a cardiac lesion are symptoms of embolism. In ulcerative endocarditis the embolism may be followed by a rise of temperature (chills and fever). Thrombosis is often preceded by paresthesias in the limbs which are about to become paralyzed, by vertigo, headache, brief impairment of speech; the apoplectic insult comes on gradually: at first only weakness and then a progressive paralysis without loss of consciousness; the hemiplegia is usually incomplete. Atheromatous condition of the blood-vessels with high blood-pressure and old age are found in softening from thrombosis. In spite of these apparently sharply defined

symptoms, there are cases in which it is impossible to distinguish between hemorrhage and vascular occlusion.

**II. Diagnosis of Hemiplegia.**—The above-mentioned differential signs may be sufficient for the determination of any given case of apoplexy. When the hemiplegia following apoplexy is definitely established but the patient falls under observation some time after the apoplectic attack, it is important to ascertain whether the paralysis is of organic or functional origin.

**A. HYSTERICAL HEMIPLEGIA.**—In hysterical hemiplegia the paralysis is usually slow and progressive, is not always confined strictly to the entire half of the body; one limb or a part of a limb is usually involved; the face most frequently is not involved, and, if asymmetry of the face is occasionally observed, it is due to a spasm but not to a paralysis. The reflexes are normal (no toe-phenomenon, no paradoxical flexor reflex, no ankle-clonus, nor any other tendon or cutaneous reflex observed in organic hemiplegia). The course of the disease is irregular: The paralysis may become ameliorated or aggravated, may alternate in its intensity, even disappear and reappear. The character of hysterical hemiplegia does not change. When the paralysis is flaccid, it will remain as such for an indefinite period of time. Spasticity does not succeed the early flaccidity, a condition which is observed in organic cases. The gait is characteristic. In hysterical hemiplegia the patient drags his leg, while in organic hemiplegia the front part of the foot sweeps the ground with each step. In hysteria there is frequently a hemianesthesia (with contraction of the visual field) on the hemiplegic side. The latter, if present, is absolute and more marked than the motor paralysis, while in organic (capsular or cortical) hemianesthesia the sensory disturbance is not evenly distributed, viz., the extremities are more affected than the trunk and the upper extremities more than the lower; also the sensory loss predominates at the periphery and decreases towards the root of the limb.

*Cerebral hemianesthesia* is usually transitory and it may last but a few hours, which is not the case with functional sensory losses. When the paralysis is spastic, the latter will remain as such until complete recovery. If, as it occasionally happens, one type of paralysis changes into the other, it is done suddenly and totally contrary to what occurs in organic hemiplegia.

**B. DIAGNOSIS OF HEMIPLEGIA ACCORDING TO THE LOCALIZATION OF THE LESION.**—(a) *Cortical Hemiplegia.*—It may present the typical form of hemiplegia or the paralysis may affect unequally the limbs on the same side, or else it may involve only one limb producing a monoplegia. The paralysis, as a rule, develops rapidly, but it may develop slowly and progressively. Subjective sensory phenomena frequently accompany the paralysis, but they are usually transitory in character. Should they persist, it is an indication of a cortical destruction in the sensorimotor region. Focal epilepsy is the result of the latter. Motor aphasia is frequent. As to the lesions, *hemorrhage* is rare, but *softening* in the area of distribution of the ascending frontal branch of sylvian artery

is frequent. In case of tumor there will be also jacksonian epilepsy.

In *tuberculous meningitis* hemiplegia is frequent: its onset is slow and insidious, involving at first the upper and later the lower extremity, rarely the face. In exceptional cases its onset is sudden and then it is preceded by convulsions. The characteristic feature of the hemiplegia is that frequently it is of very short duration, it disappears and reappears. It follows usually an attack of convulsions. In some cases, however, it may remain permanent; then it is due to a plaque of meningitis, to a localized tubercle, to encephalitis, to softening of the cortex or to a capillary hemorrhage.

Hemiplegia frequently follows a *meningo-encephalitis* of *syphilitic* origin.

*Traumatic hemorrhagic meningitis*, as well as *pachymeningitis hemorrhagica*, may be followed by a hemiplegia with the characteristics described above.

(b) *Capsular Hemiplegia*.—It is usually due to a hemorrhage or a softening in the area of distribution of the lenticulostriate artery. The paralysis is total. Hemianesthesia may accompany it because of simultaneous involvement of the thalamus. Often there are no sensory disturbances. When the postero-inferior portion of the thalamus is affected, the thalamic syndrome will be present. (See section on Thalamus.) Epilepsy does not occur, except when the hemorrhage reaches the ventricles. In the latter case there is a progressive rise of temperature and death is the usual outcome. (See section on Ventricular Hemorrhage.) In capsular hemiplegia intelligence is usually preserved, and dysarthria will be present when the knee of the capsule is involved. The speech disturbance is, as a rule, temporary.

(c) The *differential diagnosis between capsular and cortical hemiplegia* will be based on the absence of motor aphasia and of epileptic convulsions, also on integrity of intelligence in the capsular form of hemiplegia and on the presence of aphasia and jacksonian epilepsy in cortical hemiplegia. In some cases the diagnosis is very difficult, if not impossible.

(d) *Hemiplegia in lesions of other portions of the brain* will be localized according to the accompanying symptoms which are dependent upon the tissue involved. The symptomatology will vary with the extent of the lesion. It will be different in each when the lesion is in the crura, in the upper, middle and lower portion of the pons, in the upper or in the lower portion of the medulla. It will be different in the lower portion of the crura and the anterior portion of the pons and medulla than in the tegmentum. Finally the symptomatology will be special when the roots or the nuclei of the cranial nerves will be involved.

As to the lesions, they may be vascular (hemorrhage or softening), tumors or localized meningeal exudates. The vascular distribution will determine the clinical picture. The lesion may involve the basilar trunk at its origin or at its middle portion or else at the point of its bifurcation into posterior cerebral arteries. It may involve the entire vertebral artery or its branches, the anterior spinal artery, inferior and



posterior cerebellar artery. It is evident that the symptom-groups in these areas, besides the hemiplegia, will present great variations, and there will be as many combinations of symptoms as there are important cerebral portions. Thus there will be: (1) *Peduncular symptom-group*, with subvarieties depending upon whether the anterior or posterior portion of the crura is involved; (2) *Pontine symptom-groups* which, like the preceding ones, will be different for the anterior or posterior portion of the pons; (3) *Bulbar symptom-groups* which are divided into inter-olivary and retro-olivary phenomena; (4) *Diplegia*; (5) *Pseudo-bulbar symptom-group*. The multiform peculiarities and special characteristic features of each of these symptom-groups in association with hemiplegia are discussed in details in the section on Cerebral Localizations.

### MONOPLEGIA

**Diagnosis and Localization.**—The presence of a monoplegia in a paralyzed individual indicates a more exact localization of the lesion creating it than a lesion in ordinary hemiplegia. Monoplegia may be brachial, crural, facial. Similarly to what is observed in hemiplegia, the muscles are more paralyzed in the distal than in the proximal portions of the limb. Monoplegia may be partial, i.e., confined to a segment of the limb. Dejerine reports a case in which the paralysis was limited to the muscles of the forearm and hand. In Foerster's case the paralysis was limited to the muscles of the shoulder and interossei of the fingers. In fact, partial monoplegias are more frequent than total monoplegias and they occur more frequently in the upper than in the lower extremities.

Monoplegia may be *functional* or *organic*. In the latter case it may be central or peripheral.

In HYSTERIA monoplegia is quite frequent. It is almost always accompanied by anesthesia over the entire limb (sleeve-like) and the sensory disorder is more marked than the motor disorder. The entire condition is the same as that described in hysterical hemiplegia (*see* that section).

**PERIPHERAL MONOPLEGIA.**—Peripheral monoplegia may be due to a lesion of the plexuses or of the roots. In the first, we find muscular atrophy, flaccid paralysis, loss of reflexes, objective sensory disturbances, vasomotor and trophic disturbances, reactions of degeneration.

Monoplegia due to an involvement of the roots, to a *radiculitis*, presents the following syndrome isolated by Dejerine:

(a) Radicular distribution of the motor, sensory and trophic disturbances.

(b) Loss of tendon and cutaneous reflexes.

(c) Exquisite pain along the nerve-trunk of the affected limb brought on by a physical effort.

(d) Lymphocytosis of the spinal fluid probably due to the accompanying meningeal involvement.

Radicular monoplegia may be the result of trauma, of compression

of the roots by a tumor, callus or supernumerary rib, by a hemorrhage, finally by a localized syphilitic inflammation. Monoplegia may be encountered in diseases of the spinal cord, such as anterior poliomyelitis, syringomyelia, hematomyelia.

**CEREBRAL MONOPLÉGIA.**—Monoplegia, therefore, may have various origins, but the most frequent of all varieties is the *cerebral*. In the latter variety a cortical lesion is almost the only cause; capsular and subcortical monoplegias are extremely rare.

What was said with regard to certain characteristics of hemiplegia is applicable to monoplegia. It is flaccid at first, and spastic later on when the corresponding cortical center is destroyed. Not infrequently there are sensory disturbances in the monoplegic limb, which usually disappear rapidly, but in some cases persist. Atrophy may be present, but is by far not of the same intensity as in monoplegia of neuritic or myelopathic origin. The reflexes in cerebral monoplegia are the same as in hemiplegia.

As to the *localization of the lesion* of cerebral monoplegia, it is well to recall the following anatomical data:

Dejerine has shown that, in the posterior limb of the internal capsule, the fibers from the motor cortex are placed the more posteriorly, the higher they originate in the rolandic region. Thus the fibers from the operculum pass through the knee of the capsule, those from the middle portion of the rolandic region pass immediately behind the preceding ones, those from the upper portion pass posteriorly to the latter. Horsley and Beevor have shown experimentally that stimulation of the knee of the capsule produces movements of the tongue and lips on the opposite side, stimulation of the fibers back of the preceding ones produces movements of the upper extremity and stimulation more posteriorly produces movements of the lower limb. The internal capsule, therefore, has motor localizations.

Cortical localizations can be determined from the anatomy of motor centers. A crural monoplegia corresponds to a lesion of the upper portion of the ascending frontal convolution and of the paracentral lobule. A brachial monoplegia is caused by a lesion of the middle portion of the same convolution. A facial monoplegia indicates a lesion slightly above the operculum. A lingual monoplegia indicates a lesion of the foot of the ascending frontal convolution. A facial monoplegia is rarely isolated; it usually accompanies a brachial monoplegia.

## TREATMENT OF APOPLEXY AND HEMIPLEGIA

When it is DIFFICULT TO DETERMINE THE CAUSE OF THE APOPLEXY, the following measures should be applied:

At the time of the apoplectic attack the patient must be put to **bed**, clothing loosened, especially at the neck, and a free access of **fresh air** given. He must not be disturbed in the coma. The pulse and heart should be watched and according to their condition **stimulants** or **sed-**

**atives** should be administered (preferably hypodermatically). The bowels should be at once emptied by **rectal injections** and the **bladder catheterized**. With return of consciousness, the patient should be given a **fluid diet** consisting mainly of **milk**, his bowels and bladder should be closely watched and hypostatic congestion of the lung should be avoided by **changing the patient's position frequently**.

**HEMORRHAGE.**—When it is *possible to determine* at the outset the *cause of the apoplexy*, the management in hemorrhage and in softening will differ somewhat. When it is a case of *hemorrhage*, the patient's **head should be somewhat raised** and the **body placed on the back or on the non-paralyzed side**. As there are usually a flushed face and a full strong pulse, **bleeding** should be resorted to without unnecessary delay. In individuals with a strong heart 10 to 15 ounces of blood may be taken. No venesection should be practiced in cases of cardiac weakness. Lowering of blood-pressure can be accomplished not only by venesection but also by **lumbar puncture** and withdrawal of a moderate quantity of cerebrospinal fluid. **Compression or ligation of the internal carotid artery** on the side of the lesion can be used in extreme cases for arresting a hemorrhage after other measures have failed. **Puncture of the brain** has been advocated (Francke), but this procedure is dangerous. Byrne and Taylor,<sup>7</sup> however, have recently reported favorable results from **prompt operations** in intracerebral hemorrhages: Removal of a clot and of a collection of serum surrounding it was effected by the mere passage of a moderate-sized needle through the brain substance into the lateral ventricle "or in the vicinity of the internal capsule." Marie and Kindberg,<sup>8</sup> from an extensive study of anatomico-clinical cases, draw this conclusion, that the cause of coma in cerebral hemorrhages lies fundamentally in the fact that the function of both hemispheres is simultaneously suspended because of compression by the hemorrhage. Otherwise speaking, the sound hemisphere is compressed against the cranium, as well as the hemisphere which increased in volume because of the hemorrhagic content. Moreover, deep coma in apoplexy is not due to preceding cerebral lesions, to the general serious state of health, to a morbid state of viscera, to the advanced age, but to the secondary compression of the sound hemisphere and to the intensity of this compression. In view of such findings, the authors propose a **decompressive operation** on the side opposite to the hemorrhagic focus. They observed, following this operation, rapid disappearance of the coma and improvement of all the grave symptoms in a striking manner. Their advice is to operate whenever there is no return of consciousness three hours after the apoplectic seizure, also in cases in which the initial incomplete coma progressively becomes more and more profound.

The same remarks may be made with regard to certain cases of *softening* which are not accompanied by coma at first, but in which coma develops a few days later. In such cases edema develops around the initial lesion and increases to such an extent as to produce compression of the sound hemisphere.

Further *palliative* treatment is as follows:

**Ice applied to the head** may relieve congestion. As **purging** is a valuable procedure, two drops of **croton oil** should be placed on the back of the tongue. No **medication** should be given during the comatose state.

With *return of consciousness* the treatment should be *symptomatic*. Restlessness and insomnia should be combated by **bromids**, **aconite**, **trional**, **sulphonal** or **veronal**. Weakness of the heart should be treated with **mild stimulants**. Great caution should be exercised in using heart stimulants. Coffee, tea and alcohol should be avoided, unless there are special indications. Great care must be taken of the patient's **skin** in order to prevent **bed-sores**. **Bladder and rectum must be emptied** if there are no voluntary evacuations.

**EMBOLISM AND THROMBOSIS.**—When the indications are that the apoplectic stroke is due to an *embolism* or *thrombosis*, the patient's position should be somewhat different from that in hemorrhage: the **head must be somewhat lowered** or the **entire body laid flat**. **Heart stimulants** must be instantly administered if the weakness of the heart is evident or when the blood-pressure is low: **ether**, **camphor** and **nitro-glycerin** should be administered hypodermatically; **wine**, **brandy**, **tea** and **coffee** by the mouth. Application of **ice** and **venesection**, which are sometimes beneficial in cerebral hemorrhage, are contra-indicated in softening.

The further treatment of softening after the immediate symptoms have subsided should be *symptomatic*. As **internal medication**, **iodids** are advisable in both softening and hemorrhage, especially in those cases in which there are evidences of syphilitic arteritis. In cases of arterio-sclerosis with a high tension pulse, occasional administration of **nitro-glycerin** in 1-100 grain or 1-200 grain doses, two or three times a day, is advisable.

**HEMIPLEGIA.**—The treatment of hemiplegia should begin as soon as the general condition permits, and this is usually in the second week. **Passive and active movements**, in addition to **massage**, are the only means from which improvement can be expected. **Massage** is a valuable procedure, not only in recent but also in old hemiplegias with contractures. It must be given often—every day. It prevents, when instituted early, the rapid tendency to contractures, by improving the nutrition of the muscles and their tendons; it prevents ankylosis of the joints and removes the paresthesias which so frequently accompany the paralysis. Systematic **reëducation of movements** of the affected limbs is important, and this must be done with great persistence for a long period of time. Contractures may also be treated with **warm baths** followed by massage and passive movements. **Electricity** should be avoided in organic hemiplegias, as it is apt to hasten or increase the contracture of the muscles. For the same reason the drug which has a tendency to increase the tonicity of the muscles should never be given in hemiplegia, and this is **strychnia**.

To combat the rigidity of the limbs in paralysis of cerebral origin, Hoerster has devised an operation on the **spinal roots**. It will be dis-

cussed in the section on Diplegia. See also, **muscle isolation** method of *Schwab and Allison*, also that of *Stoffel*.

Franz, Sheetz and Wilson<sup>9</sup> and Elliott and Boorstein<sup>10</sup> report very encouraging results in the treatment of hemiplegic contractures by means of **tenotomies** followed by **splints** or **plaster-of-Paris casts**, and **baking**, **massage** and **slow stretching** of the limbs. As motion is gradually gained, the splints should be changed, making them straighter and straighter. The authors claim that the long duration of a hemiplegic contracture is not a contra-indication for the orthopedic treatment.

The *complications* of hemiplegia do not require special treatment. The hemi-athetosis, hemichorea and hemi-ataxia may improve with the hemiplegia itself. The aphasia which occasionally occurs depends upon the gravity of the cerebral lesion. However, attempts at reëducation of speech have been undertaken by some and fair results reported.

### SYPHILITIC HEMIPLEGIA

Syphilitic hemiplegia has been discussed in the chapter on Syphilis of the Nervous System, to which the reader is referred.

### INGRAVESCENT OR PROGRESSIVE APOPLEXY

It is characterized by sudden vertigo and headache rapidly followed by a hemiplegia. There is no loss of consciousness. Gradually the patient becomes somnolent, stuporous, comatose and dies at the end of a few days. The lesion consists of a hemorrhage caused by a rupture of the external lenticular artery. The blood spreads forward and backward and finally invades the lateral ventricles (*see* Ventricular Hemorrhage).

### DELAYED APOPLEXY

(*Spälapoplexie*)

Under this name is understood an attack of apoplexy with loss of consciousness occurring some time (but not immediately) after trauma. It was first described by Bolinger in 1891. Cases have been reported in which the interval between the traumatism and the stroke lasted from six days to four weeks. Autopsy showed, in the majority of cases, a cerebral hemorrhage. Trousseau has shown that a rupture of a blood vessel may occur some time after a concussion by means of thrombosis of capillaries, a focus of softening is thus formed in the center of which a secondary hemorrhage takes place. In the cases of delayed apoplexy the blood-vessels were found diseased (arteriosclerosis). Trauma, therefore, plays only an exciting rôle in an individual with an already altered vascular system. It is well to remember that nervous disorders occu-

ring some time after an accident are not always functional; they may be also organic and present a grave prognosis.

### HOMOLATERAL HEMIPLEGIA

Hemiplegia of the same side as the brain lesion was observed and mentioned as far back as 1845 by Nasse. Since then a number of cases have been reported at various times. As to the *pathogenesis* of this apparently paradoxical paralysis, several theories have been advanced. According to one, there is a congenital absence of decussation of motor tracts, but this, one must admit, is an extremely rare occurrence. Another view is that there is an influence of the original lesion through edema at a distance. Finally, according to a third view, there is compression of the opposite hemisphere.

The fundamental conception of hemiplegia lies in the fact that a lesion of the pyramidal pathway from the cortex to the decussation causes a paralysis of the limbs on the opposite side. Homolateral hemiplegia is only in appearance an exception to the classical localization, because in reality it is the result of a secondary lesion due to a compression of the normal hemisphere by the hemisphere containing the original lesion.

Homolateral hemiplegia never follows small peripheral hemorrhages, nor large central hemorrhages, but it is observed, on the contrary, in large meningeal hematmata, in tumors and abscesses. Consequently a slow and a diffuse peripheral compression is necessary in production of the phenomenon under discussion. The study of intracranial pressure shows that a diffuse force is necessary to displace a hemisphere, but under special conditions. The hemisphere yielding to lateral pressure meets its first obstacle, the falx cerebri. The pressure, therefore, rises in this hemisphere. The result is an ordinary hemiplegia, but if the falx is rudimentary or of small size, the compressed hemisphere moves laterally, is displaced and comes in contact with the opposite hemisphere which it presses against the wall of the cranium, hence homolateral symptoms will be the result.

Hypoplasia of the falx is not the only condition of homolateral hemiplegia. The falx cerebri is a dural partition stretched between the hemispheres. Its inferior border is posteriorly in contact with the corpus callosum, but not so anteriorly. Here it reaches the superior portion of gyrus fornicatus, sometimes the lower portion of the mesial frontal convolution, leaving open a semilunar space where the hemispheres are in contact with each other. The inferior border of the falx is usually irregular especially in its anterior portions where vascular bands connect it with the arachnoid. In aged individuals the falx is generally articulated, and through the openings the hemispheres are brought into contact with each other. In young individuals the falx is transparent and rigid. In adults and senile individuals it is thick.

It is, therefore, evident that the size, resistance and elasticity may play a certain rôle in cerebral affections. Monakow and others believe that the falx cerebri and falx cerebelli play an important part in localization of pressure.

The same author observed homolateral hemiplegia in cases with foci in occipital and frontal regions.<sup>17</sup> In Kaufmann's case, the head of the left nucleus caudatus oversteps the median line and compresses the right basal ganglia at the level of the knee of the internal capsule. Claude reports a case of tumor of the right occipital lobe resulting in a right hemiplegia.<sup>19</sup> In Monakow's case (*loc. cit.*) there was a sarcoma of the left hemisphere which, compressing the right paracentral lobule through the falx cerebri, produced spasms of the left leg.

The experimental investigations of Demole<sup>20</sup> corroborate entirely the anatomico-clinical facts just mentioned.

The conclusions to which all the accumulated data lead are that: (1) Homolateral symptoms caused by tumors, abscesses and intracranial hemorrhages are due to an indirect irritation of the hemisphere opposite the lesion. (2) This irritation usually takes place in the neighborhood of the internal capsule, although it may occur at any level of the pathway of the tracts. (3) The small size, or aplasia, of the falx cerebri facilitates the displacement of the hemispheres and consequently produces a homolateral hemiplegia.

### INTERMITTENT CLOSING OF CEREBRAL ARTERIES AND TRANSITORY HEMIPLEGIA

Besides hemorrhage, embolism and thrombosis as causes of hemiplegia, a sudden closure of a cerebral blood-vessel due to a spasm may also produce a paralysis. Bastian was the first to call attention to this condition in 1875. Not infrequently cases come under observation in which paralysis comes on suddenly and disappears rapidly. Sometimes an attack consists only of sensations of tingling or numbness in an arm or leg or in both, which may or may not be followed by paralysis or paresis on the same side. Sometimes it may be only an attack of aphasia with or without hemiplegia. The chief characteristic of these attacks is their suddenness of onset and of disappearance, also their reappearance at short or long intervals.

The spasm of an artery may produce a complete or incomplete occlusion. As a result, there is either suspension or impairment of function. The cause of the spasm lies probably in the disturbance of the vasomotor nerve supply of the arteries. The existence of vasoconstrictors has been shown by Wiggers.<sup>21</sup> Complete recovery after each of these attacks proves that the hemiparesis or hemiplegia is not due to hemorrhage or softening, but to an irregular vessel action and, therefore, to an irregular blood flow in the brain. If by proper hygienic measures the irritability of the vascular tonus can be prevented, no further attacks will occur. Otherwise it facilitates the formation of thrombosis. Recurrent attacks

may be considered as threatening or premonitory signs of eventual cerebral hemorrhage or thrombosis.

The treatment of such cases consists of internal administration of vasodilators (**nitroglycerin**), of avoidance of **emotion**, of **proper elimination** and of avoidance of **red meats**. As the disorder usually occurs in elderly persons showing evidence of arterial changes, prolonged **rest** and **potassium** or **sodium iodid** should be added to the above treatment.

### CEREBRAL ARTERIOSCLEROSIS

In the preceding section mention was made of the irritability of blood-vessels which are undergoing degenerative changes. It was emphasized that temporary and transient attacks of paresis or paralysis are produced by such blood-vessels, especially in aged individuals whose arteries are in an atheromatous state. Since arteriosclerosis leads to a poor blood supply, it stands to reason that other manifestations will be present besides temporary attacks of diminished motor power. Arteriosclerosis of the brain must necessarily present a series of disturbed functions depending upon its disturbed blood supply. The following manifestations in the psychic, motor, sensory and vegetative spheres have been observed in individuals with arteriosclerosis.

The most conspicuous evidences of the poor blood supply of the brain are *decrease in work performance, tendency to fatigue, diminution of power in association of ideas* and consequently of mental productivity and faulty memory. The individual no longer shows the former elasticity of his mind. His speech is no longer continuous, but it is halting because of lapses of memory. The progressive loss of functional capacity of the cerebrum has a great influence on his emotional life. Thus sympathy and affection are greatly diminished. The patient has crying spells, especially upon the least emotional stimulation. Headache, pressure on the head, dizziness, confusion, alternating excitement and depression, lack of orientation, are all common in such cases.

*Insomnia* is another symptom frequently observed in cerebral arteriosclerosis, probably due to cerebral irritation because of the ischemia. Poor sleep deepens the depression, so that frequently the patient becomes desperate and speaks of suicide.

The *sense of fatigue*, especially upon the least exertion, is pronounced. A distinction should be made between ordinary neurasthenia and neurasthenic complaints in cerebral arteriosclerosis. Suspicion of arteriosclerosis should arise when a man of advanced age, formerly free from neurasthenic manifestations, begins to complain of continuous and easily brought on fatigue.

The patient's *gait* is also characteristic: there is a decided uncertainty in walking, he trips frequently and stumbles, so that he fears going alone. Sometimes the gait resembles that of paralysis agitans. Tremors of the hands or of the head are not infrequently seen, especially during psychic excitement.



The sphincters sometimes suffer: *incontinence of urine and feces* are more frequent than retention.

*Attacks of apoplexy* with or without aphasia are frequent, but they are usually temporary and transient. The patient recovers, but they recur to disappear again. The frequent repetition of these attacks, which are due fundamentally to the degenerative state of the cerebral blood-vessels, eventually leads to a disturbance in nutrition of nervous tissue and to final softening (encephalomalacia) (*see* preceding section) and atrophic processes.

Cerebral arteriosclerosis, therefore, is a disease which leads essentially to serious changes in the intellectual life with a corresponding decrease in work performance, besides the various somatic disturbances and the tendency to repeated apoplectic seizures.

The *treatment* is that of arteriosclerosis in general. **Mental and physical rest.** Avoidance of **nitrogenous food.** Administration of **nitrites and iodids.** Every effort should be made to reduce high blood-pressure.

### MENINGEAL HEMORRHAGE

Anatomically there may be several varieties:

(1) **Cerebro-subarachnoid Variety.**—In this variety meningeal invasion originates from the brain or ventricles.

(2) **Meningocerebral Form.**—In this form the subarachnoid hemorrhage is primary and the cortex is secondarily involved.

The outlook in the first variety is more serious than that in the second. Besides, in the cerebromeningeal variety there is a history of diseases of the heart, blood-vessels or kidneys, a chronic disease of the nervous system, a toxi-infectious process or finally a trauma of the cranium.

(3) **Meningo-encephalitis in Young Individuals.**—Apart from these conditions, there is a group of cases in which meningeal hemorrhage may occur *spontaneously in young individuals* free from hereditary or personal predisposition and without visceral lesions. Such patients may improve and recover, but may also, after a more or less long interval of good health, have recurrences which eventually will terminate in a fatal hemorrhagic encephalitis (Chauffard, Froin and Boidin;<sup>22</sup> Cordier, Lévy and Nové<sup>23</sup>). The PATHOGENESIS of this condition can be determined by analogy with attacks of hemoptysis in pulmonary tuberculosis. It is due to processes of congestion. Microscopical investigations show that at the periphery of the hemorrhage there are discrete but undoubted lesions of endophlebitis and endarteritis, dilatation of capillaries, and above all a considerable infiltration of leukocytes in the perivascular spaces. All these findings indicate the presence of an encephalitis. The pathogenic mechanism is analogous to that of non-traumatic hematomyelia, in which a primary, inflammatory process in both vessel-wall and nervous tissue leads to the apoplectic form of acute myelitis.

As to the CAUSE of the hemorrhagic meningo-encephalitis in young

persons, analysis of the recorded cases points to a toxi-infectious process. At autopsy old lesions of the meninges are seen, i.e., thickening at various levels with newly formed blood-vessels; infiltration with leukocytes in the perivascular spaces indicates a transitional stage between the meningeal and encephalitic lesions.

In view of these anatomical data the above-mentioned possibility of



FIG. 4.—EXTENSIVE MENINGEAL HEMORRHAGE OVER RIGHT PARIETAL LOBE.  
(Gordon, Courtesy *Archives of Internal Medicine*.)

improvement and recovery from spontaneous hemorrhagic meningitis must not lead to an absolute optimism and, therefore, to a favorable prognosis. The toxi-infectious process, the fundamental cause of the condition, will produce, in the majority of cases, not only a meningitis but also an encephalitis, and the spontaneous onset of the meningeal hemorrhage is only apparent because the infectious state is still in existence. That meningeal hemorrhages are curable must be admitted only in a relative sense and only for an immediate prognosis. But, as mentioned

above, recurrences are the rule and then, instead of the meninges alone, the cerebrum itself will also be invaded by the toxi-infectious process. The pathological susceptibility of the meninges in young individuals is peculiarly great and encephalic involvement should be suspected at greater or less intervals after the initial attack on the meninges. The prognosis, therefore, in spontaneous meningeal hemorrhage must be made with great reservation.

Besides this special form of meningeal hemorrhage leading to hemorrhagic encephalitis, extensive hemorrhages in the meninges may occur in pernicious anemia, leukemia, scurvy, infectious diseases, such as typhoid and small-pox, and renal diseases.

Virchow always believed that in all these cases there is a toxemic alteration of the dura. Other authors believe that the disease produces a pathological state of the vessel-wall which leads to rupture.

**SYMPTOMS OF MENINGEAL HEMORRHAGE.**—They are chiefly those of intracranial pressure. In cases of slow development *somnolence* is the most conspicuous early manifestation. The pupils are contracted. Epileptiform convulsions appear early. Hemiplegia or monoplegia is present when the central convolutions are involved. Bradycardia and hyperthermia are constant symptoms. Kernig's sign and rigidity of the neck are present.

(4) **Meningeal Hemorrhage Due to Trauma.**—In traumatism of the head that produces fracture or infraction of the cranial bones, the middle meningeal artery, passing externally between the cranium and dura and dividing into anterior and posterior branches, is frequently injured. The clinical picture is as follows: At first there may be no special SYMPTOMS except signs of concussion. The patient may even get up and walk. Gradually, however, and sometimes several hours later, symptoms of intracranial pressure will appear: headache, vertigo, vomiting, slow pulse, etc. As the extravasation of blood increases, epileptiform convulsions and paralysis will make their appearance on the side opposite to the seat of the hemorrhage.

The present war has supplied a very large variety of cranial injuries. In some of them meningeal hemorrhages occurred without fracture of the skull. In such cases the symptomatology may be slight, viz., slight mental confusion, some headache, inequality of the pupils and bradycardia, but a lumbar puncture will reveal a hemorrhagic or xanthochromic appearance of the spinal fluid.

In cranial contusions there may be a subdural hematoma, which may disappear spontaneously or after lumbar punctures.

In making a diagnosis of traumatic meningeal hemorrhages, besides the classical symptoms (headache, rigidity of the neck, Kernig's sign, bradycardia, etc.), the following additional symptoms will be of value: cerebral excitement with confusion; the *contralateral reflex* of Guillain, which consists of flexion of the opposite limb if one limb is pinched or pressed upon (the knee, for example, flexes and the foot scratches the stimulated part). It is a true *defense reflex* and is observed especially in the first phase of the affection, while the patient is in the comato-

state. In some cases the color of the skin is yellowish, probably due to hemolysis and absorption of its products (Guillain, Troisier, Laroche). G. Guillain<sup>24</sup> calls attention to a special phenomenon which he observed in some cases of hemorrhagic meningitis. It is a *massive albuminuria* of 2 to 20 grams per liter, appearing very rapidly, i.e., twenty-four or forty-eight hours after the onset of the affection, but then rapidly diminishing so that at the end of a few days it may disappear. This albuminuria is not accompanied by edema of the limbs or viscera, or by arterial hypertension; the urine does not contain blood or casts; otherwise speaking, the albuminuria is not the result of renal insufficiency. It is probably of central origin. It seems that the disturbance in renal secretion permits the passage of albumin in the urine because of the transitory changes in the cranial or spinal nerves. The blood in the pia-arachnoid cavity is capable of developing meningeal symptoms, such as Kernig's sign, contractures of radicular origin and basilar disturbances analogous to those observed in infectious meningitis. It is, therefore, conceivable that local disturbances of basilar or spinal nerves are one of the factors of renal vasomotor disturbances which lead to albuminuria. It is to be borne in mind that albuminuria is of diagnostic value in hemorrhagic meningitis only when it is abundant (massive).

**TREATMENT.**—In meningeal hemorrhages due to fractures of the skull and in those without fractures, the condition of the meninges controls in the beginning the entire symptomatology and the immediate prognosis. The early coma, epileptic seizures, pupillary disturbances, bradycardia, etc., etc., are all dependent upon the presence of blood in the subarachnoid cavity. It is, therefore, of the greatest importance to make a diagnosis as rapidly as possible for immediate therapeutic efforts as well as for the individual's future.

The only treatment in cases of meningeal hemorrhage is naturally an **operation**. The latter must be performed by an osteoplastic resection over the area which the diagnostic elements prove to be compressed. The sooner the operation is performed, the better the results to be expected, as recovery is possible. The longer the brain pressure has persisted, the more unfavorable is the outlook.

(5) **Meningeal Hemorrhage Following Explosions, but without External Injury.**—The first records of meningeal hemorrhage following deflagration of explosives are cited by Ravaut.<sup>25</sup> Since then a large number of observations have accumulated in the literature. Laroche, Léri, Guillain, Barré and others reported many instances of hemorrhages in the central nervous system. These facts observed during the present war prove conclusively that it is an error to consider all the cases of concussion of the brain as being of a functional character (hysteria).

**SYMPTOMS.**—An analysis of the cases reported shows the following features: The diagnosis of meningeal hemorrhages and of the presence of blood in the cerebrospinal fluid could be made from the clinical symptoms, lumbar puncture being only confirmatory. The general symptoms described in the preceding section (headache, hyperesthesia, Kernig's sign, bradycardia, etc.) were all present. There were also: cerebral irri-

tation with mental confusion, the contralateral reflex (Guillain), disturbed pupillary reactions; yellowish pigment of the skin. Hyperthermia was present in a certain number of cases for several days. Elevation of temperature has a prognostic value, as in grave cases it is high.

The majority of these cases improve and complete recovery has been observed in a few instances.

The PATHOGENESIS of meningeal hemorrhages following explosions without external injuries can be explained on the following premises: deflagration of heavy quantities of explosives liberates a considerable amount of gas, which, being projected, repels the atmospheric air under high pressure. The increased pressure of air created by the explosion is succeeded by a depression. The hyperpressure seems to be an important factor in the labyrinthine disturbances met with so frequently in concussion (Bourgeois and Sourdille<sup>26</sup>). On the other hand, that atmospheric depression exists is proved by the facts that, during the explosions, the soldiers were drawn toward the site of the explosion. A similar phenomenon is observed in the *aéronauts*, also in the caisson disease (visceral hemorrhages after rapid decompression). Sudden death has been observed in soldiers after violent explosions and other soldiers are stunned and remain fixed in one position from the same cause. Death is probably due to liberation of gases in the blood and formation of gaseous emboli because of the great depression.

The accidents of concussion may be also explained by an abrupt distention of the circulatory apparatus, by sudden pressure on the surface of the body and especially on the abdomen, all the blood of which is driven to the deep parts, especially to the central nervous system. This vascular distention may be observed in the fundus oculi (Lépine<sup>27</sup>).

Experimental work was done by Prénaut and Castex<sup>28</sup> on rabbits and guinea-pigs which thus were rendered deaf by violent explosions. Histological examinations showed cochlear dislocations, atrophy of Corti's body, hemorrhages in the tympanum and occasionally an ascending degeneration of the cochlear nerve.

In the experiments conducted by Mairat and Durante<sup>29</sup> autopsies showed foci of pulmonary apoplexy through rupture of alveolar capillaries, hemorrhages on the surface of the spinal cord, hemorrhages in the roots, rupture of small blood-vessels of the gray substance of the cortex and medulla. The smallness of the hemorrhages speaks in favor of sudden rupture of the vessel-wall through abrupt depression. The hemorrhages do not act by compression of neighboring organs, but produce local anemia with subsequent softening. The authors conclude that the symptoms observed in soldiers have an organic origin in spite of the fact that there was no external injury at the time of the explosion.

The results of careful observations, clinical and experimental, show conclusively that violent explosions are apt to produce organic lesions of the central nervous system, either small hemorrhages or cellular and nerve lesions. One must be very cautious in making a favorable prognosis in the beginning of the concussion, because, if in some cases r

covery is obtained, in others cicatrices are formed in the nervous tissue and as sequelæ lead to serious disturbances in the function of the limbs. All these disturbances are not always due to hysterotraumatism or to simulation. The reality of organic lesions in these cases is proved by the course of the disorder, by the distribution of paralytic phenomena, by changes in the reflexes and by the findings in the cerebrospinal fluid. The nervous manifestations are analogous to those observed in divers' disease, in individuals working in compressed air and constantly submitted to abrupt modifications of atmospheric pressure. (*See also* section on Concussion.)

(6) **Pachymeningitis Hemorrhagica Interna or Hematoma of the Dura.**—The disease is rare and met with in extreme ages of life, viz., in very young children and aged individuals. It occurs not infrequently in the insane and especially in paretics. Alcoholism (chronic) is a very frequent etiological factor. Rheumatic diathesis, infectious diseases, traumatism, are other causes of hematoma of the dura.

**PATHOLOGY.**—The chief lesion lies between the arachnoid and the dura and consists essentially of a thickening of the latter and formation of layers of membranes on its inner surface to which they adhere. The membranes are very vascular. The new blood-vessels of this new tissue have external and internal coats, but no media, a condition which makes them fragile. Rupture of the new blood-vessels, which frequently undergo degeneration, is the origin of the blood found in pachymeningitis. The blood accumulates between the laminae of the newly-formed membranes. The amount of blood varies from a very small quantity to a very large collection. The hemorrhagic cyst thus formed may undergo transformations, among which the most important are serous, purulent (through secondary infection) and a state of calcification. It goes without saying that the brain tissue will suffer from compression caused by the adherent cyst; inflammation with softening will be the result. The most frequent seat of the hematoma is the parietal lobe; then, in order of frequency, come the temporal, frontal and occipital lobes.

**SYMPTOMS.**—When the hematoma is very small, the pachymeningitis may pass unobserved, but most of the time the hematoma reaches a sufficient size to present symptoms of cerebral compression. In the majority of cases prodromal symptoms are present. They are: headache, vertigo and a paralytic condition accompanied by convulsions on one side. Headache may be the only symptom for some time. It is very severe, localized on one side of the skull and usually not accompanied by fever. The pupils are, as a rule, contracted, but more on the side of the lesion. Nystagmus may be present. Edema of the papilla is frequently observed and it is due to the compression; it has the same value as in tumors of the brain with this difference, that it appears late in the course of pachymeningitis. Gradually, and sometimes rapidly, coma makes its appearance; at first it is only slight, but gradually becomes more and more profound. Death supervenes, usually in a short time. The paralysis may affect one or two limbs, also the face.

The palsy is rarely complete. Its onset is slow but progressive. In cases with a slow onset, a gradually increasing mental hebetude with great somnolence is the most striking feature. In a case of a physician who died from this affection, there was noticed an extraordinary tendency to sleep; he would fall asleep wherever he happened to be. It was also noticed that he was unable to concentrate his attention. Gradually he developed unilateral convulsions, an exaggerated knee-jerk on the same side, also the paradoxical reflex. An extensive hematoma of the dura was found on the opposite side.

**PROGNOSIS.**—In all cases the outlook is very grave. Recovery is extremely rare. Remissions may occur in the course of the disease, but death is the usual termination. The duration is from a few weeks to several months.

**DIAGNOSIS.**—Mental hebetude, somnolence, headache with localized palsies and convulsions may be met with in *cerebral syphilis*. The paroxysmal character of the headache and its aggravation at night, finally the history of a specific infection, will differentiate brain syphilis from hematoma of the dura.

It was mentioned above that the paralytic symptoms develop gradually in hematoma of the dura. This will differentiate the latter from cerebral hemorrhage in which the apoplectic seizure and the hemiplegia appear suddenly.

*Tuberculous meningitis* may sometimes simulate internal hemorrhagic pachymeningitis, but the less acute headache, constipation, retraction of the abdomen and the character of the cerebrospinal fluid of the former will render the diagnosis less difficult. The greatest difficulty is experienced in making a diagnosis between hematoma of the dura and cerebral tumors. In such cases it may be of some use to remember that edema of the papilla is a very frequent occurrence in tumors. It is less frequent in pachymeningitis and it appears quite late in the latter disease.

**TREATMENT.**—**Counter-irritation, leeching** in the mastoid regions, **elevation of the head, ice to the head, avoidance of stimulants**, are all the means used in such cases. If there are strictly localized symptoms, **evacuation of the hemorrhagic focus** is advisable. In the case mentioned above, the first operation gave excellent results: the patient rallied and the headache disappeared.

(7) **Meningeal Hemorrhage in the Newly Born.**—**ETIOLOGY.**—Hemorrhage in the meninges of the newly-born follows all varieties of deliveries. It is due to trauma of labor, instrumental or natural. Forceps delivery through a contracted pelvis is the commonest cause. At first there may be no symptoms; the latter appear usually on the second day and sometimes later. Cases are known in which hemorrhage occurred with smooth normal deliveries in women with wide birth passage and normal pelvis, who had already borne children. Mayer<sup>30</sup> report 12 such cases, remarking that they show that there must be some predisposition on the part of the children. It is possible that letting the child lie on its side may compress the veins and induce venous hy

peremia, thus aggravating a tendency to hemorrhages in the tentorium region which the newly-born might otherwise survive. Pressure from accumulated blood explains the cases in which slightly asphyxiated newly born children become more and more asphyxiated and explains also the sudden deaths of not asphyxiated newly-born who seemed to be normal for a time and then died suddenly.

**SYMPTOMS.**—The intracranial pressure produced by the hemorrhage does not present, as a rule, the clinical picture ordinarily found in adults. The reason of it lies in the fact that the sutures and bones of the infant's skull are distensible and this factor plays a part in the delay of the manifestations characteristic of intracranial tension. However, experience teaches that if a baby within a few days of birth begins to refuse the breast and, according to Green, shows edema of the face, the presumption is in favor of intracranial hemorrhage. Rapidly other symptoms make their appearance: the skin is very pale; respiration and pulse are irregular; reflexes are increased; convulsive movements appear in the face and limbs and are very frequent; they are followed by a paretic condition of the latter; finally bulging of the fontanels completes the clinical picture. Lumbar puncture is a necessary procedure in diagnosis of the seat of the hemorrhage. In supratentorial hemorrhage the blood is over the convexity of the brain and no blood is found in the spinal fluid. In the infratentorial cases, the blood is in the subarachnoid space and extends to the base, covering the medulla, cerebellum and entering the spinal canal, so that lumbar puncture will reveal the presence of blood in the spinal canal.

The symptoms will, therefore, vary *according to the seat of the hemorrhage*. With hemorrhage above the tentorium the symptoms are more of a cortical nature, principally in the domain of the facial, oculomotor and accessorius nerves and in the extremities; the children are restless and scream from the stretching of the dura, the greater fontanel bulges, and the vagus center, the vasomotor center and respiratory center show signs of irritation.

With hemorrhages below the tentorium, the symptoms are from the spinal nerves, such as rigid extremities, erection of the penis and wrinkling of the skin on the scrotum. The children are strikingly quiet and somnolent and early show cyanosis; the fontanels do not bulge and the spinal fluid is not bloody. In doubtful cases, puncture of the subdural space through the large fontanel at a point farthest toward the side may decide the question.

**MECHANISM OF FORMATION OF HEMORRHAGE.**—The general opinion is that the meninges are the usual source of the hemorrhage. Beneke<sup>31</sup> believes that, in the majority of instances, the lesion is a laceration of the tentorium. In Pott's 33 autopsies on the new-born, lacerations of the tentorium were found either at its free edge, or on its superior layer, or else between the layers. He explains the lacerations by the tension on the tentorium along the long axis caused by compression during parturition. In cases without lacerations of the tentorium the hemorrhage may be due to rupture of the pial veins (Hen. Hen.).



Besides meningeal hemorrhages, bleeding may occur in the ventricles. In such cases, its origin is probably from the veins of the choroid plexuses. When the hemorrhage is supratentorial, the blood may originate from lacerations of the superior longitudinal sinus (Seitz). In the infratentorial hemorrhages the small veins ending in the lateral sinuses, or else the sinuses themselves, may be torn.

**FREQUENCY OF OCCURRENCE.**—Hedren, of Stockholm, found intra-cranial hemorrhage in about 9.28 per cent. of 700 infant cadavers. The hemorrhage was restricted to the meninges in nearly 84 per cent and cerebral hemorrhage accompanied by meningeal hemorrhage in others, bringing the total of meningeal hemorrhages to 90.7 per cent. Delivery had been spontaneous in 50 of the 65 cases, and conditions in both mother and child seemed to be normal in most of the cases. In the 42 purely meningeal cases, the hemorrhage had been supratentorial in 32; infratentorial in 10, and both kinds in 6. He ascribes the great causal importance to intra-uterine disturbances in respiration and circulation, as well as to compression of the bones of the head in the birth passage. Only 3 of the children presented unmistakable evidence of inherited syphilis. In a few of the cases the mother had eclampsia.

**TREATMENT.**—On the first suspicion of a hemorrhage a **lumbar puncture** should be made. Green<sup>32</sup> and Lippman<sup>33</sup> report complete cures from one or several lumbar punctures. French writers have published many successful cases of this kind. This procedure may be extremely useful in infratentorial hemorrhages. In the supratentorial hemorrhages, as described above, no results can be expected from this method, and one must have recourse to **cranial puncture**. Giles<sup>34</sup> advises **puncture of the fontanel** by means of the Pravaz needle. The needle is introduced to a depth of 5 or even 8 mm. as far from the longitudinal sinus as possible in the frontoparietal angle of the fontanel. This draws a certain amount of blood at once before it has had the time to clot, and the rest is easily absorbed. Puncture of the fontanel is merely an exploratory operation, but it may have an actual curative value. If, however, no relief is obtained, **craniotomy** or incision through the coronal suture preceded by **aspiration of the subdural space** should be undertaken. Of 9 cases operated on by Cushing<sup>35</sup> 4 recovered, and of 3 operated on by Murphy 1 recovered.<sup>36</sup>

The most important consideration should be given to *prophylaxis of intracranial hemorrhages*. In normal deliveries one should avoid strong compression of the head with the hand. High forceps application should be avoided as far as is reasonably possible. Cesarean section should be preferred to high forceps. On the other hand, protracted labor with the fetal head undergoing considerable compression at the brim of the pelvis may be more injurious and present a greater predisposing element for meningeal hemorrhage than instrumental interference. Prompt intervention with any procedure described above will save life and in many instances prevent the probable develop-

in the child's later life of spastic paralysis, diplegia, epilepsy, and also mental defects.

## THROMBOSIS OF THE INTRACRANIAL SINUSES

**Varieties.**—Two varieties of sinus thrombosis are to be distinguished: *primary or marantic* and *secondary or inflammatory or infective* (thrombophlebitis).

A. **MARANTIC THROMBOSIS** occurs in individuals with a low vitality, as in tuberculosis, cancer, chlorosis, protracted diarrhea or in any disease of long standing during which malnutrition and exhaustion are conspicuous. It occurs most frequently in children and in the aged. The cause of the thrombosis lies in the weakness of the heart produced by the severe diseases, and, therefore, in retardation of circulation and increase of the coagulability of the blood. Its seat is usually in the longitudinal and transverse sinuses.

B. **SECONDARY OR INFLAMMATORY OR INFECTIVE THROMBOSIS** is due to a lesion in the neighborhood of the dura. Inflammation of the latter is usually the result of the direct contact with the diseased area or it is due to an infection carried through the veins to the sinus. Thrombophlebitis follows diseases of the skull, face or ear. Caries of the petrous bone is frequently the cause. In the latter case, the lateral, superior and inferior petrosal sinuses are affected. Diseases of the cranial cavities, of the pharynx and mouth, periostitis of the maxillary bones, erysipelas of the face, are all causes of thrombophlebitis.

**Pathology.**—The thrombus presents a grayish or red clot adherent to the walls of the sinuss. It may affect only a part of the sinus or occupy its entire length and even extend into the tributary veins. The resulting venous stasis produces hyperemia and extravasation; edema is considerable. The ventricles are distended. Softening of the cerebral substance follows. If both transverse sinuses are occluded, the entire brain will suffer. If only one is occluded, there will be some compensation. When the longitudinal sinus is occluded, there can be no compensation.

The phlebitis, which causes thrombosis, may suppurate. The thrombus is then purulent and metastases are often seen in various organs; cerebral abscess or purulent meningitis may follow.

**Symptoms.**—They are *general* and *special*.

The **GENERAL SYMPTOMS** are: mental hebetude, somnolence, headache associated with vomiting, rigidity of the neck and of the extremities, sometimes convulsions. Optic neuritis is frequently present, especially in cases of chlorosis. In infective thrombosis there are also rigors followed by profuse perspiration and rise of temperature; edema in the vicinity of the sinus; sometimes pain in the abdomen and diarrhea; restlessness and delirium in some cases.

**SPECIAL SYMPTOMS.**—They depend upon the sinus involved.

1. **Longitudinal Sinus.**—Engorgement of the temporal veins; cyan-

nosis of the face, in the region of anterior facial vein; tension of the large fontanel in children; because of the distention of the veins of the nose, epistaxis is present.

2. *Transverse Sinus*.—The internal and external jugular veins are less filled than those on the sound side. The mastoid region is edematous and painful.

3. *Cavernous Sinus*.—Since the ophthalmic vein flows into this sinus, also because of communication of the ophthalmic vein with the anterior facial vein, there will be: stasis and edema in the ophthalmic vein, edema of the orbit and eyelids, exophthalmos, congestion of the



FIG. 5.—THROMBO-PHELEBITIS OF RIGHT CAVERNOUS SINUS.

(From Gordon's "Diseases of the Nervous System," P. Blakiston's Son & Co.)

retinal blood-vessels and edema of the disk. Paralysis of the third and sixth nerves, also of the first branch of the fifth nerve, is frequent.

EYE SYMPTOMS are important from a diagnostic standpoint. In the marantic form they are not as frequent as in the infective form:

(a) In the *marantic form* the following eye disturbances are sometimes met with: venous stasis and hyperemia in the fundi, optic neuritis, fixed pupil. Conjugate deviation of the eyes is present when the longitudinal and transverse sinuses are simultaneously involved. When the cavernous sinus and the ophthalmic vein are involved, exophthalmos will occur. The third nerve is oftener affected than the others.

(b) In *infective thrombosis* eye symptoms are very frequent. According to Uhthoff, hyperemia of the papilla, optic neuritis, fixed pupil and optic atrophy occur in 20 per cent. of cases. Involvement of the cavernous sinus in septic thrombosis occurs in 80 per cent. This explains the frequency of eye disturbances. Exophthalmos is the most

frequent symptom. Uhthoff observed it in 72 per cent. When the sphenoid bone is affected, the exophthalmos is bilateral. Palsy of the ocular muscles is almost a rule when the cavernous sinus is involved, because of the proximity of the sinus to the third, fourth and sixth nerves. Facial neuralgia is present (first branch of the fifth nerve).

In sinus thrombosis of OTITIC ORIGIN visual disturbances and changes in the fundi are of diagnostic value. The latter are frequently bilateral, as in other intracranial affections. Immobility of pupils develops rapidly. Jansen found fixed pupils in 30-40 per cent. Optic atrophy, according to Uhthoff, is found in 24 per cent. Exophthalmos is less frequent in thrombosis of otitic origin than in other septic forms of thrombosis.

**Course and Prognosis.**—The *marantic form* is insidious in onset and long in duration. Death is the usual termination. The *infective form* has a different course. Sudden onset, chills, violent headache and very high temperature are all indicative of a purulent state. Its duration is usually a few days. It may be complicated by an abscess in the temporosphenoidal lobe.

**Diagnosis.**—Appearance of cerebral symptoms in an individual suffering from any of the diseases mentioned in the beginning of this section should arouse suspicion in regard to phlebitis and obstruction of sinuses. The following chief features will serve as a guide in DIFFERENTIATING the *marantic form* from the *infective thrombosis*: The usual seat of the first is the single sinus, i.e., longitudinal; the seat of the second is in bilateral sinuses. The first has a tendency to become organized and absorbed; the second has a tendency to suppurate. In the course of the first, cerebral hemorrhages occur; in the second, hemorrhages are rare. The first has a tendency to softening, which is not the case in the second. Septic metastatic infections are frequent in the second, not in the first. Purulent meningitis and cerebral abscess are common in the second, absent in the first (Macewen).

**Treatment.**—**Preventive measures** are most important. The strictest attention should be given to diseases of the ear and other organs, to avoid secondary infection. The **medical treatment** of the thrombosis is purely *symptomatic*. In the *marantic form* **tonifying** measures are necessary. **Rest in bed** is essential. **Surgical treatment** is advisable only in the secondary form of thrombophlebitis. **Opening and curetting of the affected sinus** may sometimes be of benefit.

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## CHAPTER VI

### ENCEPHALITIS

By H. H. HOPPE, A.M., M.D.

Exudative encephalitis, p. 597—Acute hemorrhagic cortical encephalitis, p. 598—Polio-encephalitis superior or Wernicke's disease, p. 607—Epidemic lethargic encephalitis (epidemic stupor), p. 608—Tuberculous localized meningo-encephalitis, p. 609—Encephalitis of the new-born, p. 612—References, p. 613.

We shall distinguish in treating the subject of encephalitis between the two chief groups of this disease: namely, the exudative and the non-purulent hemorrhagic forms. Strictly speaking, the term encephalitis should be restricted to those forms in which inflammation is the chief pathological change. We cannot, however, exclude the tuberculous form of encephalitis, because it offers a clinical and pathological picture very different from tuberculous meningitis. Syphilis, which is a common cause of meningo-encephalitis, must be considered under the head of Cerebro-spinal Syphilis.

So, also, those various forms of encephalitis and cortical degenerations, occurring during intra-uterine life or in the new-born, so varied in their pathological aspect, but so similar in their clinical picture, are more satisfactorily treated under the chapter of Cerebral Palsies of Childhood.

We shall consider, therefore, the exudative, the non-purulent hemorrhagic, the tuberculous form of encephalitis and lethargic encephalitis.

### EXUDATIVE ENCEPHALITIS

**Etiology.**—In all forms of encephalitis, especially in the exudative form, although the chief lesion is located in the gray matter of the cortex, there is always an involvement of the overlying pia mater. We usually have, therefore, a localized and circumscribed meningo-encephalitis. The bacterial cause in these exudative forms is either the staphylococcus, streptococcus or pneumococcus, and the source of origin may be a focus of pus anywhere in the body.

**Pathology.**—The exudate is serofibrinous, with a marked extravasation of the leukocytes, and, according to Macewen, of minute punctate hemorrhages, which may coalesce and give the appearance of the hemorrhagic form. It is difficult to separate these two (the hemorrhagic and the exudative) forms pathologically, as well as clinically. On the other hand, if the exudative is very profuse, the pathological picture may

approach that of a superficial subdural abscess. Macewen also speaks of a white softening of the cortex, due to a predominance, in the infiltration, of leukocytes. This form is usually embolic in origin. In one very acute case, running its course in 3 to 4 days, the macroscopic appearance of the brain was apparently normal, but the microscopic examination showed the characteristic changes of encephalitis.

Only pathologically is there a distinct difference between the exudative and the hemorrhagic non-purulent encephalitis. Clinically, except at times in an etiological sense, there is very little difference between the two forms. Clinically, therefore, we will consider them together.

### ACUTE HEMORRHAGIC CORTICAL ENCEPHALITIS

This variety of encephalitis is called by the German authors the "Strümpell-Leichtenstern form." Strümpell<sup>1</sup> first directed the attention of the medical world to this subject by his paper on infantile cerebral palsies, as being frequently caused by encephalitis, and many years before this (1865) Virchow<sup>2</sup> had made exhaustive studies of the pathology of encephalitis of the new-born.

In 1885, Leichtenstern<sup>3</sup> described a case of acute non-purulent encephalitis occurring during the course of an epidemic of cerebrospinal meningitis, and he was the first to call up the thought that the disease was due to an infection. The influenza epidemics of 1889-1891 brought out typical cases; those of Fürbringer,<sup>4</sup> of Königsdorf,<sup>5</sup> and Schmidt<sup>6</sup> deserve special mention.

**Etiology.**—After the *bacteriological origin* had been denied by Strümpell, Brickler, Goldscheider and others, although in the typhoid, diphtheritic and other zymotic diseases, streptococci had been found, Pflügl, and especially Nauwerk, by finding Pfeiffer's influenza bacillus, were enabled to furnish the proof that the disease was due very often to direct bacterial invasion of the brain and not to ptomain or leukomain intoxication, or to secondary infection.

The etiology of acute hemorrhagic encephalitis of the cortex is usually directly or indirectly *bacteriological or zymotic*. Either the inflammation is due to the direct invasion of the cortex of the brain by the bacteria which cause the primary disease, as for instance in influenza, where we have positive evidence, or in diphtheria and typhoid, where we surmise, although as yet the bacteria have not been demonstrated; or it is due to the peculiar zymotic agency or to the ptomains of the other acute infectious diseases, when it occurs as a complication of measles, scarlatina, etc.

Whether *alcohol*, *ptomain poisoning* from fish or from meat, or any of the *metallic poisons*, can produce an acute encephalitis of the cortex of the brain, as they are supposed to do in the gray matter of the pons or cord, the author doubts. Alcohol is the most common direct or indirect cause of Wernicke's form of encephalitis. We should, however, feel inclined to place infection and contagion as the primary, if not the

only, cause of encephalitis of the cortex; although in some of the reported cases of Wernicke's disease—15 in all, according to von Monakow—the cortex and the gray matter of the basilar ganglia have occasionally been involved.

The two sexes are often equally affected. If all cases were published, the writer has no doubt that the period from early childhood up to puberty would be found to be most frequently affected, principally because the *acute infectious diseases* are most frequently found at this period of life. Most reported cases are found in adults. General weakness and loss of strength do not seem to be predisposing causes, for, like cerebrospinal meningitis, primary encephalitis is very frequently seen to attack strong, robust individuals, previously healthy. The amount of general exhaustion during the course of an infectious or contagious disease does not seem to bear any relation to the probability of an intercurrent or subsequent encephalitis. Encephalitis of the cortex is most frequently seen during the course of *influenza epidemics*. During such epidemics primary encephalitis is frequently seen where the influenza attacks the brain alone, or, to express it more appropriately, the predominating symptoms are on the part of the brain, with an absence of respiratory or intestinal symptoms. Encephalitis may occur during an attack of ordinary influenza, or it may follow in the course of a few days or even after weeks or months after the attack of influenza.

Encephalitis may occur during an *epidemic of cerebrospinal meningitis* without any involvement whatever of the meninges. Of the acute infectious diseases, we should say that *measles* is most frequently complicated with encephalitis; next in order *typhoid*, *scarlatina* and *diphtheria*. In these diseases it usually occurs when the disease itself is on the wane, or during convalescence.

*Trauma* is a frequent cause of acute hemorrhagic encephalitis, and in a two-fold way: First, in a purely mechanical way. The brain is either bruised by concussion, and then a reaction of inflammatory softening occurs. Second, without any fracture whatever, the bruised brain cortex becomes the seat of a circulatory infection: micrococci, which are circulating in the blood, are deposited and set up an inflammation in the bruised spot.

**Pathological Anatomy.**—Viewed in its relation to the immediate and remote effects of encephalitis, the pathological anatomy can be considered from two standpoints, the acute stage and the residual stage.

According to Fürbringer, who described the first cortical cases, the most frequent form of acute encephalitis in the cortex, as well as in the gray matter around the canal of Sylvius, is the acute hemorrhagic form. The macroscopic appearance of encephalitis is that of circumscribed areas varying in size from a pinhead to a silver dollar. They are multiple, rarely single, and are often symmetrical in distribution. These areas are most frequently met in the cortex, but are found also in the white matter and in the basilar ganglion. They are bright red in color in the recent cases, but the color varies as the blood-pigment changes in color to a purple-brown, yellowish-brown, or yellow. The area is



more succulent than the surrounding tissue, because it is infiltrated with serum, and is slightly raised above the general level of the surrounding cortex and, macroscopically at least, the margins are somewhat sharply defined. Microscopically, there is a dilatation of the arterioles and capillaries; a transudation of red and white blood-corpuscles into the surrounding tissue; and later on, pigment particles, phagocytes, and an increase of the spindle cells. (See Figs. 1 and 2.)

Like anterior poliomyelitis, the disease is, by consensus of opinion,

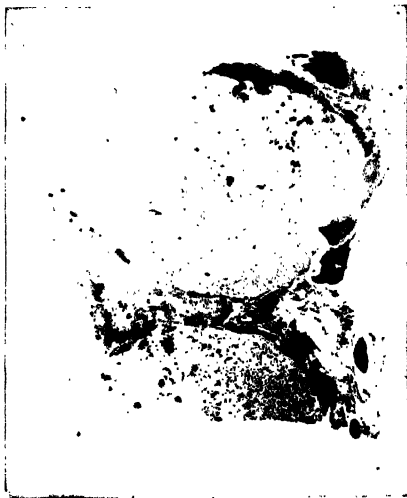


FIG. 1.—HEMORRHAGIC ENCEPHALITIS.

supposed to be vascular in its origin. What is more interesting is the fate of the nerve elements, cells and fibers in the area of this acute inflammation. The ganglionic cells are affected, but only secondarily; the protoplasm becomes swollen, more translucent; the nucleus less distinct; afterward the cells become more opaque; occasionally the protoplasm is seen to break up; and there seems at times to be a total destruction of cells, at others the cells shrink, become deformed, and the nucleus becomes crenated. But this is not a parenchymatous process; it is interstitial in its nature. Aside from the hemorrhagic form, Oppenheim has described a yellow or white inflammation in which the macroscopic appearance shows an absence of the engorgement of the arterioles and capillaries, and an absence of the transudation of the red blood corpuscles. In other respects, the microscopic anatomy is the same.

The above processes, both the hemorrhagic and non-hemorrhagic, may terminate in a complete *restitutio ad integrum*. This is shown, in

only by the clinical cases in which there has been a complete recovery from all symptoms, but more satisfactorily, by the case observed by Oppenheim. This case was that of a young girl who completely recovered from an attack of encephalitis, and died six months later of another disease. The autopsy made by Oppenheim showed a complete absence of all traces of the former encephalitis.

Far more frequently, in the favorable cases which terminate in recovery, some defect of the cortex is found, which is the cause of either



FIG. 2.—HEMORRHAGIC ENCEPHALITIS. SECONDARY MENINGITIS.

the incomplete recovery from paresis or of the subsequent development of epilepsy.

The first of these defects is the formation of scar tissue which is seen very frequently. Nerve fibers, especially tangential fibers, are involved in the scar, according to a case reported by Buchler. Strümpell contends that the cortical scars in children's palsy are due to this form of encephalitis. The second is the formation of cysts. Cortical brain tissue shows a variation in its reaction to inflammation from the other tissues of the body. In the latter the tendency is to form scars; cysts, however, are formed in the brain, which frequently enlarge by a continuous breaking down of their walls.

The pia mater is adherent over some of the cysts. Microscopically there is found in the wall granular debris, leukocytes, a few red blood-corpuseles, disintegrated ganglionic cells, giant cells, very little connective tissue.

There cannot be much doubt but that cysts have their origin very frequently in acute hemorrhagic encephalitis. This opinion is backed up by Bergmann in a paragraph devoted to the discussion of the treatment of Strümpell's form of porencephalic defects, in which he speaks of the possibility of these late permanent cysts, which occasionally follow encephalitis, being the cause of cortical epilepsy and therefore objects of surgical interference. Starr, in "Brain Surgery," publishes a similar case, and Henschen and Dahlgren have collected 17 cases of a similar character, which have been operated upon.

That multiple sclerosis may be the late stage of encephalitis is a possibility; but that the clinical disease which we know under this name is the same is very much doubted, the consensus of opinion being that it is a disease of a different origin.

Oppenheim calls attention to the fact that encephalitis is frequently associated with sinus thrombosis and thrombosis of veins, but usually in cases in which clinically there was a well-marked chlorosis.

**Symptomatology.**—Clinically we can hardly establish a difference between the various forms of acute encephalitis as distinguished by their etiological factors. We shall attempt to draw a clinical picture which will cover both *the exudative and the non-purulent hemorrhagic forms*.

The symptomatology is varied, but the numerous signs and symptoms can easily be grouped under three heads, or rather into three periods in chronological order, namely: (1) the period of onset and development; (2) the period of focal signs and symptoms; (3) the permanent signs and remote consequences.

The first and second groups overlap each other more or less, but are sufficiently distinct to be separated.

The general symptoms may be preceded by indistinct prodromal symptoms for a day or two, such as headache, vertigo, general malaise, but as a rule the onset is sudden, rarely with a chill, usually with a high fever or the exacerbation of a previously existing fever. There is rapid development of mental symptoms, and the climax is reached in from twenty-four hours to four or five days or a week. The developed mental symptoms resemble very closely an attack of acute delirium tremens, so much so that Werneke, who recognizes chronic alcoholism as the most potent factor of encephalitis hemorrhagica superior, at first was inclined to attribute the mental characteristics to chronic alcoholism rather than to encephalitis. Bödeker showed, however, that this mental state occurred in encephalitis of the cortex without there being any evidence of chronic alcoholism.

The onset in primary encephalitis is usually sudden, with headache, and vertigo, and a sense of general malaise. A chill, sometimes though not often, ushers in the rise of temperature, which is at once high— $102^{\circ}$  to  $104^{\circ}$  F. ( $38.9^{\circ}$  to  $40^{\circ}$  C.)—with rapid, small pulse. Restlessness and a desire to move about precedes the delirium; collapse is not frequent. After the development of the delirium, nearly all cases present the same manifestations, the differences in the writer's experience being

one of degree and not character. Restlessness, jactitation, sleeplessness, hallucinations both aural and ocular, together with those of general sensation, keep the patient on the alert. Frequently there is a constant muttering of incoherent sentences; not infrequently there is a response to the aural or ocular hallucinations, calling to supposed friends, answering voices which the patients think they hear; often, maniacal character of movements or speech, constant rambling conversation, smoothing bed sheets, picking bed clothes, removal of imaginary bugs. In the course of from two to five days the delirium gradually subsides, the hallucinations and responses to them are not so clearly defined, the speech becomes muttering and incoherent, the acuteness of the fire being smoldered by a blanket of increasing somnolence. The patient frequently becomes lucid, at intervals, answers questions promptly and correctly; but these intervals last only a very short time. During all these days, the temperature is high; the pulse rapid; the breathing rapid and superficial; there is no, or very little, retraction of the head, though opisthotonos does at times occur, herpes does not develop, and there is no eruption on the body. Sordes of lips and teeth are marked. As a rule, there is no change in the pupillary reaction, although in some cases there is an inequality; light reaction is usually present, at times absent. Choked disk is always absent in the cortical form; external muscles of the eyes are not involved. Reflexes vary, sometimes normal, often increased; some cases are ushered in by general or unilateral convulsions, especially in children. In the very violent cases, sopor and coma set in and mask most of the localizing symptoms. In the milder cases, improvement usually sets in before the somnolence becomes very marked. In the state of coma, there is an involuntary discharge of feces, retention and incontinence of urine, and at times bed-sores. Death occurs from exhaustion.

In those cases which develop during the course of one of the febrile diseases, there is sudden exacerbation of fever, the pulse becomes rapid, the patient complains of headache and dizziness and then almost at once, at least in a few hours, the delirium sets in and the above symptoms may all be developed; or the disease runs a milder course, with delirium, restlessness, insomnia, together with the hallucinations and muttering.

During the course of the delirium, in some cases before it reaches its height, in others after the somnolence has set in, the second group of symptoms is developed. Whether or not these continuous cases of delirium and coma may be looked upon as a manifestation of frontal encephalitis remains to be seen by future pathological observations. The first of these signs is paralysis. The onset is very sudden, but paralysis is rarely complete; or if it is complete, it very rapidly improves during the course of the first few days.

Aphasia, both motor and amnesic, and paraphasia are seen very frequently as focal symptoms of encephalitis.

In favorable cases, the general symptoms clear up, the sensorium becomes free after two to three weeks. The focal symptoms remain

for some time longer. They may completely disappear in the course of weeks or months, or there may be a permanent defect; and this leads us to the third stage, which is not present in those cases in which the recovery from the inflammation has been complete. The paresis which remains is more or less spastic in character. Contractures, with a retardation in general development, are seen frequently in the cerebral palsies of children.

In adults the paresis may manifest itself as a slight weakness and awkwardness of the arm, or leg, or entire side.

The author's experience with aphasia was that the speech showed some defect, even a long time afterward. The most serious of all the sequela, however, is the development of epilepsy: either jacksonian, which is usual, or general epilepsy, which is the exception.

**Course, Duration and Termination.**—The course of acute non-purulent encephalitis of the cortex is that of the ordinary acute infectious disease. Fever is at times absent, but usually a high fever, and all the characteristics of the onset of an acute infectious disease mark the beginning. The main symptoms of the disease, the involvement of the sensorium, viz., the acute delirium, restlessness, insomnia, hallucinations, followed by progressive somnolence and sopor, and finally coma, show at once the seat of the disease to be in the cortex. The height of the disease is usually reached in three to four days; then the mental excitement gradually subsides.

Even during the delirium, most frequently during the somnolence, the focal signs make their appearance. After ten to twelve days the case may end fatally; or improvement takes place, and in a week the sensorium is clear and the focal signs are already waning. Cases are on record in which death has taken place within twenty-four hours, in other cases in three to four days; the ordinary duration of the primary acute cortical encephalitis is from two to four weeks. Those which complicate acute febrile diseases are somewhat shorter, but only apparently because the convalescence of the two diseases is merged together. When death occurs in encephalitis, it is due either to the shock of the onset or to toxemia in the very acute stages; again, death is often due to the spread of the disease to vital centers, occurring most frequently as a result of the involvement directly by inflammatory process of the respiratory or cardiac centers.

In cases which run a favorable course, the coma scarcely ever supervenes, even the sopor does not become profound; the case continues for some days, perhaps a week, in a state of mild delirium, with moderate fever and a rapid pulse; when the fever and delirium subside the sensorium becomes clear; the patient shows mental confusion, does not remember clearly the events of the foregoing days; nothing remains aside from this but great exhaustion and the focal signs, which gradually diminish.

**Diagnosis.**—The diagnosis of the cortical form of encephalitis is much more difficult than that of Wernicke's disease. The differential diagnosis of acute non-purulent cortical encephalitis must be made from

*abscess, meningitis, uremic focal lesions, cerebrospinal meningitis, acute mania, hemorrhage and thrombosis.* The adult form is here referred to. In children it must be separated from *acute gastro-intestinal disturbance*. When the trouble occurs as a primary affection or as a sequela, the diagnostic difficulties are most marked. The most important thing is to rule out *cerebrospinal meningitis*. The latter disease is usually characterized by the extreme violence of the headache, and the tendency to spastic rigidity of the extremities; the opisthotonos is very marked, there is a spastic condition of arms and legs, and Kernig's sign is never absent. There is present the delirium and high fever, but the maniacal signs are more marked in encephalitis, the headache is not so severe, opisthotonos is usually absent, and retraction of the head, if present, is only indicated slightly. Symptoms and signs on the part of the cranial nerves, involving especially the third nerve, facial and lingual, are the rule in leptomeningitis; whereas, in encephalitis, these are either absent or only present in one group of muscles, and unilateral. The author would lay a great deal of stress on the absence of violent headache and the absence of irritability of eyes and ears, especially during states of delirium, and the absence of uniformly exaggerated reflexes, especially during the delirium or sopor stage.

Cerebrospinal meningitis may occur sporadically, but as a rule it occurs in epidemics; whereas primary encephalitis occurs most frequently during the prevalence of grippe epidemics. Symptoms occurring as sequela of some one of the acute diseases would make us suspect encephalitis rather than cerebrospinal meningitis. Monoplegia and aphasia are apt to occur during an attack of cerebrospinal meningitis, but never stand out as prominently, nor do they occur as early; in encephalitis, on the other hand, they occur early and assume the most prominent phase. Herpes does not occur in encephalitis.

*Uremic focal lesions* should be differentiated from first and foremost by a careful urinalysis, but since albumin is sometimes absent in uremic cases, other points would have to be considered. Encephalitis, in the adult at least, where uremia might enter most into consideration, is rarely ushered in by a convulsion; whereas, in uremia convulsions are the most prominent feature and occur in rapid succession. Uremia, in the early stage at least, occurs without fever; encephalitis corticalis is rarely without it. Uremic focal lesions occur sometimes before, but mostly during the coma period, and usually disappear with the coma, or in a few hours or days; whereas, in encephalitis, the focal lesions do not usually make themselves manifest for two to three days, and persist for a long time—weeks or even months.

It is most difficult to differentiate between encephalitis and *acute mania*. This cannot be done sometimes for several days. The presence of a continuous fever speaks for encephalitis; moreover, encephalitis is more apt to give the impression of a severe somatic disease, which makes the patient bedfast and exhausts him; whereas the mania case, at least in the beginning, impresses us as more of a mental and less of

a physical disease. The onset of the focal signs places the diagnosis of encephalitis beyond question.

*Abscess* might cause some trouble, especially in those cases where the encephalitis occurs as a complication of one of the acute infectious diseases. An abscess is very rarely sudden in origin, whereas, encephalitis usually is; in encephalitis general symptoms, especially those on the part of the sensorium, are more marked, in abscess they are usually absent, except in the advanced or final stage. The difficulty can be present only in the early stage of either disease, not in the later stages, and the writer would place most stress on the condition of the sensorium. Furthermore, in abscess some local or distinct focus for pus is invariably to be found, or at least a history of some injury, usually recent in date.

*Hemorrhage* and *softening* are somewhat difficult to rule out in the primary affection, for both hemorrhage and cerebral softening usually occur, especially with the typical alterations of the sensorium, as sudden attacks but without prodromata and fever. Moreover, encephalitis usually occurs in individuals with normal vessels and arteries.

When encephalitis occurs during, or as a sequela of, one of the *acute infectious diseases*, it is always accompanied by an exacerbation of the fever and delirium; hemorrhage or softening which might occur during the same disease usually is not accompanied by fever or delirium. Oppenheim says that the coma of encephalitis is never as deep as that of hemorrhage, and that the pupillary reflex is usually present. Cerebral syphilis is ruled out by the occurrence of a febrile disease.

**Treatment.**—The treatment varies with the cause. The most important step is to introduce rapidly into the circulation of the patient remedies which may tend to destroy the germs which are the cause of the encephalitis.

In the influenza cases, this is **benzoate of soda** in 15-grain doses, every two hours, by mouth. Small doses of **calomel** will also be of assistance when the bacterial cause is unknown. It has been the author's custom to give large doses of **sodium salicylate** by rectum—viz., 75 grains (4.86 grams) of sodium salicylate; 20 drops of tincture of opium dissolved in starch water (one pint)—twice a day, for four to five days. At the same time intramuscular injections of bichlorid of mercury (grain  $\frac{1}{4}$ ) have been given for three days in succession. An **ice-bag** to the head may give relief for the head pains and delirium. **Chloral** and **bromids** may combat the restlessness; **morphin** and **hyoscin** should be given only as a last resource. After the disease has run its acute course, **iodin** in some form should be given for weeks or even months, more especially in cases in which motor or aphasic symptoms continue, if the febrile disturbance has subsided.

**Prognosis.**—In the early stage of our knowledge of encephalitis it was looked upon as almost invariably fatal; but with a broader knowledge of diagnosis, it has been found that the disease very often runs a favorable course, especially where it occurs as a sequela or complication of typhoid or the acute infectious diseases. Pathologically, we can have one of three sequelæ, either complete restitution, the formation of a scar,

or the formation of a cyst. These latter conditions are the causes of the permanence of the focal signs, or what is equally if not more important, the causes of subsequent jacksonian or of general epilepsy. In recovered cases, the mental condition is usually good. There may be some of the forms of aphasia, which may lead us to suspect an apparent mental defect. The focal signs usually show decided improvement. In some cases there is left a slight trace of paresis; and in the aphasia cases there may be some defect left in speech years afterwards. On the other hand, von Jaksch looks upon the prognosis as bad, and doubts the correctness of the diagnosis of the cases which have ended in recovery. In the writer's opinion, the prognosis is worse in influenza cases, the result being, as a rule, fatal. The author's experience is that the prognosis of non-purulent encephalitis is not altogether unfavorable; at times the disease terminates favorably. Bad prognostic signs are: influenza, rapid onset and short duration of delirium state, with rapid onset of the coma: Cheyne-Stokes respiration, and high temperature. If the delirium is light, the sensorial depression not deep, and the mental symptoms begin to clear up in a few days, the prognosis is good. A very rapid pulse is a bad sign.

The best prognostic indications, therefore, are to be gleaned from the conditions of the sensorium. General conditions must be taken into consideration. During the course of an exhausting disease, this general exhaustion may be a bad prognostic sign. But like epidemic cerebrospinal meningitis, strong, healthy individuals may be fatally attacked.

Oppenheim says that in the vast majority of cases we can make only a problematical diagnosis.

## **POLIO-ENCEPHALITIS SUPERIOR OR WERNICKE'S DISEASE**

In this connection we will consider only the symptom-complex described by Wernicke and in which the lesion is limited to the gray nuclei of the third nerve and the gray matter of the thalamus. Other acute encephalitic lesions of the brain stem, occurring either alone or in conjunction with anterior poliomyelitis, will be considered under the head of bulbar diseases.

Gayet first described this syndrome, but it was not until 1881, when Wernicke's textbook with a complete anatomical and clinical description appeared, that the disease became generally known. The mental and physical picture was later elaborated by Bödeker and Bohnhöffer, who called attention to the resemblance of the mental phenomena of delirium to Korsakoff's psychosis, which, together with the rapidly developing ophthalmoplegia, gives the clinical syndrome such striking characteristics that it can hardly be mistaken for any other disease.

**Etiology.**—Some cases have been described as occurring on a non-alcoholic basis, but they are not well authenticated and few in number. The usual and, in fact, constant cause is chronic alcoholism. It occurs



usually in male patients who have been addicted to excessive alcohol indulgence for many years.

**Pathology.**—Why the gray nuclei of the third nerve and the adjacent gray matter of the thalamus should be the seat of predilection for the pathological changes is a mystery. That the changes are more extensive, and probably vascular in origin, is more than probable when the mental symptoms are taken into consideration. Capillary hemorrhages probably take place in various parts of the cortex, but are most marked in the gray nuclei of the third nerve. There is no true inflammation with exudative changes, but vascular lesions with hemorrhages which destroy the gray matter. Southard suggests the analogy between this lesion and the characteristic hemorrhages in anaphylactic intoxication.

**Symptomatology.**—The symptom-complex is characterized by a sudden attack of delirium, without fever, which closely resembles delirium tremens. There may be general malaise, headache and vomiting for some days preceding the delirium. The delirium itself is characterized by mental hebetude and physical exhaustion. Very soon after the onset of the delirium the patient develops more or less complete bilateral ophthalmoplegia with ptosis of both eyelids. The optic nerves are also involved, the retina showing hemorrhages in many of the cases, and the papillae, a mild degree of optic neuritis.

In a general way there are muscular weakness and an ataxic gait.

The disease is progressive. The delirium gives way to drowsiness, and later stupor and death take place in from 10 to 14 days.

**Diagnosis.**—The DIFFERENTIAL DIAGNOSIS must be made especially from Korsakoff's polyneuritis psychosis, because the prognosis in the latter condition is essentially more favorable.

The differential diagnosis is made by the more gradual onset of Korsakoff's disease. In the latter the symptoms of poliomyelitis with general paresis in the extremities, hyperesthesia of the skin and tenderness of the muscles on pressure usually precede the development of the mental symptoms for days and weeks. Moreover, the mental symptoms are milder, and do not resemble active delirium tremens as closely as do those of Wernicke's disease. In Korsakoff's polyneuritis, the ophthalmoplegia is not often found; whereas in Wernicke's disease it is the characteristic lesion. General muscular tenderness is usually absent in Wernicke's disease.

**Prognosis.**—The prognosis is usually bad. Cases have been known to recover, but death usually takes place in coma in from 10 to 14 days.

## EPIDEMIC LETHARGIC ENCEPHALITIS

(*Epidemic Stupor*)

Acute encephalitis in epidemic proportions was observed first in France and in England early in the year 1918. It is supposed to be similar to a mysterious epidemic, observed in Italy in 1890, called

"nona." This epidemic has been variously called epidemic stupor, acute infective ophthalmoplegia, acute encephalitis and botulism.

**Etiology.**—The etiology is doubtful. While, in this epidemic, a considerable number of persons had recently partaken of sausages, shrimps, lobsters, canned salmon, cheese, the majority had not, and no particular food could be connected with any of the cases. No bacteriological evidence of botulism were demonstrated. An attempt was made to connect this disease with epidemic poliomyelitis, but no cases of the latter character were found during this epidemic. Prof. Arnold Netter<sup>7</sup> reports that the spinal fluid is negative, both for bacteria and chemically. The cases were observed in Paris and in large numbers in London, but isolated cases occurred all over England and Wales. Of 105 cases, 64 occurred over the age of 20; but children in the first year of life—even a breast-fed infant of 3½ months—were also affected. Lately, epidemic lethargic encephalitis has been observed all over the United States.

**Symptomatology.**—The author has seen no records of autopsy, but the clinical history points to an encephalitis which must closely resemble Wernicke's disease.

In 87 cases<sup>8</sup> closely studied, 41 cases presented fever; in only 8 cases was it stated that there was no fever. Headache and profuse sweating were present in about one-third of the cases. Drowsiness, lethargy, stupor and coma were present in nearly all; in only 9, however, did actual coma occur. Delirium was present in 20 cases; vertigo in 17. The paralysis of the eye-muscles, ptosis, strabismus, diplopia, complete paralysis of all the external eye-muscles and nystagmus are seen in the majority of the cases. The internal eye-muscles are not so often affected, although there may be paralysis of accommodation and slow light reaction. Bilateral facial paralysis was noted in 9 cases, and unilateral facial palsy in 11 cases. The tongue and the extremities are affected only exceptionally; opisthotonos and Kernig's sign are present in only a few cases.

Obstinate constipation is frequent and vomiting is present in some cases.

The duration in some cases may be only a few days; in other cases it may last for six weeks.

During convalescence the asthenia and the muscular weakness persist for a long time.

**Prognosis.**—The prognosis is grave, 20 per cent. ending fatally.

## TUBERCULOUS LOCALIZED MENINGO-ENCEPHALITIS

Meningo-encephalitis is at times of tuberculous origin. It is usually located in plaques on the convexity of the brain and produces the symptoms of a focal disease rather than those of a diffuse meningitis. This is a subacute or chronic form of encephalitis.

**Etiology.**—It may be a local manifestation as secondary to tuberculosis elsewhere, or it may, according to Gougert and Combe,<sup>9</sup> be the

only manifest lesion of tuberculosis. Combe, however, insists that adults are more frequently affected. It is most dangerous for children.

**Pathology.**—Raymond and Alquier<sup>10</sup> describe the meningo-encephalitic process as characterized mainly by a great proliferation and formation of new vessels with a special increase in the thickening of the intima, and secondarily, by a marked perivascular exudate, with a massive pouring out of lymphocytes. The exudate shows a rapid tendency to necrosis and degeneration. This exudate may show a tendency to the formation of small tubercles, but often, according to Gougert,<sup>9</sup> the non-follicular form is frequent; the exudate is diffuse and breaks down very readily; and the presence of tubercle bacilli can be easily demonstrated. Combe<sup>11</sup> says that these plaques vary in size and that they consist of fused granulations and fibrinous deposits. The pia over these areas is thickened and contains miliary tubercles. The pia over the rest of the brain is either normal, or it may be thickened. The base of the brain is normal. Gougert<sup>9</sup> divides the case anatomically into acute, subacute, and chronic. In the acute form, the infiltration is accompanied by punctate hemorrhages with rapid necrosis and degeneration of the tissues; whereas in the more chronic forms there may be a hypoplastic necrosis of tissues with subsequent sclerosis. Gougert looks upon tuberculosis as one of the most frequent causes of encephalitis.

**Symptomatology.**—Clinically we have the picture of the subacute or chronic development of cortical focal lesions, with daily elevation of temperature, general convulsions or jacksonian seizures, spastic monoplegias or hemiplegias, and contractures. The course may be a chronic one. The cerebrospinal fluid may be of diagnostic value in so far as no other bacteria are found to explain the disease. On the whole, the diagnosis is very obscure and we cannot be positive without confirmation by autopsy.

The disease is so rare and so obscure that the author does not hesitate to illustrate it with the clinical history of a case in which the diagnosis was made during life. The child being still alive, the diagnosis cannot be confirmed.

**CASE:** Infant, 17 months of age. Colored. Cincinnati General Hospital. (Fig. 3.)

Child ill for six weeks with bronchopneumonia.

On admission, January 23, 1918, fairly well nourished, had rapid respiration, restlessness, temperature 100° F. (37.8° C.), pulse 152, respiration 154.

*Examination on Admission:* Eyes reacted to light and accommodation, no strabismus, no nystagmus. Objective signs of bronchopneumonia. Examination of nervous system negative, with an absence of all objective signs. The history, however, showed that six weeks before, while on same service, patient had a general convulsion with fever.

*One week after admission,* patient had two general convulsions twenty-four hours.

*After an interval of one week,* another convulsion occurred, two

utes in duration, followed by a tonic spasticity of muscles of neck, arms and legs, no Kernig's signs, no Babinski. Spinal fluid under pressure. Wassermann negative. Fluid clear and negative for bacteria.

*In the next twenty-four hours* child developed a left-sided hemiplegia, spastic in type, with positive Babinski. Gradually right side was also affected with spastic contractures. Kernig's sign positive. Cerebrospinal fluid, 80 cells per cu.mm. Wassermann negative. Continuous elevation of temperature, rapid pulse. Cerebrospinal fluid negative for meningococci and pneumococci.

*Neurological Examination*, February 26, 1918 (one month after admission to pediatric service): Child partially conscious, because it cried when undressed. Child's head retracted, occiput turned toward left shoulder. Vertebral column rigid and arched and turned also to left.



FIG. 3.—CASE OF TUBERCULOUS MENINGO-ENCEPHALITIS.

Left arm spastic and contracted. Left leg held rigid and in extreme extension. Foot in extreme plantar extension, with flexure of toes.

On crying, deficiency of expression on right side of face was noted. Tongue in median line, in mouth. Left side of tongue flattened, as compared to right. Conjugate deviation of eyeballs to right, which was not varied by attracting attention of child to light, except momentarily. Pupils equal, medium in size and did not respond to light.

Right hand contracted also. Rigidity of right shoulder girdle. Right hand held in condition of extension, hand flexed on forearm, forearm on arm, but fingers in extension, more especially index finger, which was separated from the rest of them. Same condition in left arm only more marked.

Normal fundi were found.

Spastic rigidity of leg marked, so that it could not be overcome, to determine whether child had clonus or plantar reflex.

*Diagnosis:* Tuberculous meningo-encephalitis en plaque; perhaps sub-entorial.

*Course:* Condition remained unchanged for 60 days and then gradually improved under mercury and arsenobenzol. During the 130 days spent in the ward, he had a daily rise of temperature varying from

97° to 101°-102° F. (36.1° to 38.3°-38.9° C.), even to 106° F. (41.1°C.). He was discharged with all motor symptoms still remaining, but a general improvement present, and a decrease in spasticity.

*Temperature Record*

On admission .....	99.4°	Fahrenheit
1st day .....	104.2°-100.2°	"
2nd " .....	105° -100.8°	"
3rd " .....	101.6°- 99.8°	"
4th " .....	102° - 99°	"
5th " .....	101.6°- 99.6°	"
6th " .....	101° - 99°	"
7th " .....	99.8°- 99°	"
15th " .....	103° - 98.6°	"
23rd " .....	102.8°- 98.6°	"
40th " .....	101.4°- 97.8°	"
59th " .....	101.8°- 97.4°	"
80th " .....	100° - 97°	"
91st " .....	106° - 97°	"
108th " .....	101° - 97°	"
117th " .....	105° - 98.4°	"
126th " .....	99.2°- 97.2°	"
130th " .....	99.2°- 97.6°	"

The chief characteristic of this case is the slow onset of the focal signs, preceded for two months by an attack of general convulsions. The very slow progress of the disease; the occurrence of convulsions during its course; the development of focal signs; the continuous presence of fever which could not be accounted for on any other basis except a brain lesion; the very chronic course; the child being under observation for 150 days; the negative bacterial findings in the spinal fluid, and above all the repeated negative Wassermann reaction of the spinal fluid after use of mercurial injections and the intravenous use of arsphenamin.

### ENCEPHALITIS OF THE NEW-BORN

Undoubtedly encephalitis occurs in the fetal state, as well as after birth. In its cause and pathology it does not differ from the forms described above, and the clinical picture which follows the pathological defect is that of cerebral palsy. The pathology of cerebral palsy of children, however, is far more extensive than that of encephalitis, including as it does teratological defects of development due to asphyxiation during birth, cortical hemorrhage due to intra-uterine trauma, difficult birth or forceps injuries. For this reason mere mention of the form of encephalitis, without any further attempt to treat the subject more fully, is made in this chapter. That encephalitis is a frequent cause

of stillbirth, more especially when the mother has had one of the acute infectious diseases toward the end of the term of gestation, is a contention made by Virchow and by others who followed him in this line of research and investigation. But this matter has not been definitely settled.

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## CHAPTER VII

### ABCESS OF THE BRAIN

By H. H. HOPPE, A.M., M.D.

**Bergman's classification of abscess of brain,** p. 615—Traumatic abscesses, p. 615—Abscesses due to purulent inflammations of the bone, p. 625—Tuberculous abscesses, p. 627—Metastatic abscesses, p. 627—So-called idiopathic abscesses, p. 628.

Abscesses of the brain present greater difficulty of diagnosis, and call for more experience and more judgment than do brain tumors and cysts. There are two difficult problems presented by abscess of the brain which are much more difficult than the same problems in tumors and cysts: viz., (*a*) to determine whether or not an abscess is present; (*b*) to locate the abscess. This is more especially true of latent or chronic abscesses. The symptoms of brain abscess are not only frequently obscure and indefinite, but for a considerable period of time, even for years, may be absent altogether. In tumors and cysts time is relatively not so important; a few days or a few weeks may elapse and the diagnostic points may be allowed to develop themselves. In abscesses, however, time is of the greatest importance; a few days, even twenty-four hours, may determine whether or not an individual's life can be saved.

The subject of abscesses of the brain is even more important than the subject of tumor: for, whereas, only a small percentage of the latter are the subject of radical surgical intervention, every case of abscess of the brain is, at least in theory, operable and without surgical intervention is doomed to death.

**Bergman's Classification of Abscess of the Brain.**—According to their origin Bergman divides brain abscesses into four groups, and, for the purpose of studying the difficulties in the latent period, the consideration of the etiology offers the best results.

1. Traumatic abscesses caused by an open scalp wound or a fractured skull.
2. Abscesses resulting from a purulent inflammation of bone or bony cavities: (*a*) otitic abscesses; (*b*) rhinogenic abscesses; (*c*) abscesses due to caries of the bones of the skull.
3. Tuberculous abscesses.
4. Metastatic abscesses.

#### 1. TRAUMATIC ABCESSSES

Traumatic abscesses are of two kinds: (1) superficial, dural, or subdural, acute abscesses; (2) subcortical, with a more or less latent period



between the occurrence of the trauma and the development of symptoms of cerebral abscess.

These two forms of abscess present an entirely different clinical history.

**Etiology.**—Traumatic abscesses presuppose a direct communication between the cranial cavity and the external world. Fracture of the skull is usually present, but at times only a scalp wound, and in some rare cases only a contusion of the scalp have been present as the entering source of the infection. There must always be, as a rule, an open channel of infection. Abscesses may follow fractures at the base of the skull, the open channel then being the auditory canal, nasal cavity, frontal sinus or pharynx.

In recent abscesses, following soon after an injury, the source of infection is usually very apparent; but in latent abscesses, the original injury may not be mentioned, or the symptoms of fracture of the skull may have been very obscure. An abscess of the brain always presupposes the presence of the pus-forming organism. This enters the brain directly through an infected wound, the infection spreading through the fracture and setting up a localized, purulent inflammation and the formation of a surface abscess. In cases in which we have a scalp wound without fracture, the organism probably travels by the way of the veins of the diploë, thence to the dura. The organism then enters through the perivascular lymph spaces and gives rise to a subcortical abscess, with an apparently normal layer of gray cortex between the abscess and the pia mater. At times the source of infection may be distant, one case being seen by the writer in which the source of pus was an infected bruise over the tibia. In gunshot wounds the infection is carried to the brain by the bullet, which carries with it fragments of the skull or a piece of scalp. In stab wound the blade is sometimes broken off, and remains in the brain. In other fractures of a violent character, shell fragment for instance, small spicules of bone may be driven into the brain. The wound itself often shows no external sign of infection. Macewen calls attention to the fact that penetrating stab wounds are more often followed by abscesses than more severe and comminuting fractures, because the latter can be and are usually given more careful surgical attention than the former.

Concussion and contusion of the brain, no matter how serious, are never followed by an abscess, unless there is an open scalp wound or a fracture of the skull.

With the wider application of the principles of asepsis and disinfection of wounds, the traumatic abscesses are becoming less frequent.

Traumatic abscesses usually develop very soon after the trauma but an interval of months, or even years, may elapse, the abscess becoming latent.

The abscesses, both superficial and subcortical, are usually found immediately under the seat of the injury; but there are cases on record in which they have been found on the opposite side of the brain, and cases in which occipital injuries have been followed by frontal ab-

scesses, or *vice versa*. We can explain these very rare cases only on the theory that the pus organisms were brought through the general arterial circulation to a contused area.

**Pathology.**—**SUPERFICIAL ABSCESSSES.**—In superficial subdural abscesses we have a localized meningo-encephalitis (Fig. 1). The inflammatory area becomes localized, and the seropurulent exudate accumulates between dura, below the pia; gradually the free purulent exudate increases in amount, and produces irritation and compression of the cortex of the brain. Unless surgical relief is given at this time the inflammation extends and a general purulent leptomeningitis follows. We should bear this in mind especially in relation to the so-called cases of



FIG. 1.—ACUTE LOCALIZED PURULENT MENINGITIS.

sympathetic meningitis, cases which occur as complications in acute mastoid or ethmoid disease. The inflammation in these cases is always at first localized, circumscribed and serous in type. But if the underlying cause is not relieved, we quickly have a purulent meningo-encephalitis, as is proven by the increased cell count of the cerebrospinal fluid. This is followed by a general purulent leptomeningitis.

**DEEP ABSCESSSES.**—Deep abscesses may occur soon after the exciting cause, or they may occur after an interval of months or even years. If they occur soon after the accident, the clinical history is somewhat different than if months or years elapse.

The pathology of deep abscesses varies as to whether they are recent or latent.

*Recent abscesses* are subcortical, with a normal layer of gray matter separating them from the pial covering (Fig. 2). In all probability, the pus-forming organism gains access to the brain tissue through the perivascular lymph spaces; only in exceptional instances are they brought

directly through the general circulation. The size of the abscess varies. In the very acute processes no limiting membrane is formed; the purulent exudate infiltrates, and forms an abscess without the limiting membrane. If the process is less acute, an exudate of fibrin is thrown out about the purulent exudate. This becomes organized and forms a tough fibrous membrane which shuts off the pus, and the abscess becomes *latent*. After a latent period of more or less duration, the limiting membrane is pierced and traversed by the pus-forming organisms. A purulent softening is set up in the brain tissue outside of the membrane, which extends to the surface, perforates the gray matter and

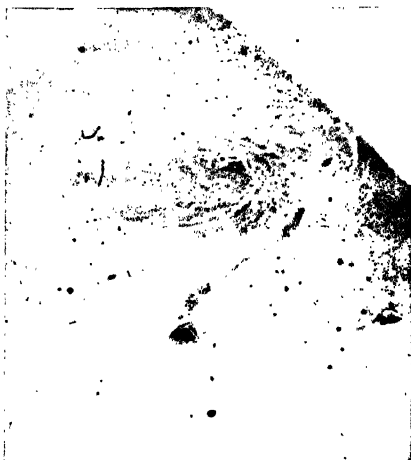


FIG. 2.—BRAIN ABSCESS.

sets up a purulent leptomeningitis which is at first localized, but soon becomes general and causes the death of the patient. In other cases rupture takes place through the walls of the lateral ventricle and rapid death, at times in a few hours, occurs, as a result of pressure on the floor of the fourth ventricle, the pus passing through the canal of Sylvius. At times rupture of the abscess is preceded by the development of a meningitis sympathetica. Strauss\* looks upon the occurrence of the latter as an aid to diagnosis of brain abscess. The cerebrospinal fluid is then under greater pressure; it is turbid, shows an increased cell count, is sterile.

The location of the latent abscesses varies with the cause. Traumatic abscesses are more common over the parietal and frontal regions because this region of the skull is more susceptible to accident.

**Symptomatology.**—**SUPERFICIAL ABSCESES.**—A few days or a few

\* Am. Jour. Med. Sci., Nov., 1917, 748.

weeks after a scalp wound or fracture, the patient begins at first to have general manifestations which can be classed under two heads: (a) infection; (b) localized meningo-encephalitis.

The disease often is ushered in by general malaise, chill, rather high temperature and rapid pulse. Then the meningeal symptoms appear; headache which is violent and general, with local symptoms of increased pain and tenderness over the seat of the previous scalp wound or fracture. Delirium and general restlessness set in after a few days, or even hours. This is followed by periods of stupor, during which, however, the patient can be aroused, and made to give an account of the symptoms.

If the abscess is located over the so-called *silent areas*, we do not have focal symptoms. But if it is located over the psychomotor areas or other specialized areas, focal signs are very quickly developed. We may have localized jacksonian seizures which may, and usually are, at first strictly local, and are followed by paresis, and later on by spastic monoplegia or hemiplegia. In other cases we may have one of the various forms of aphasia, varying with the location of the abscess, with or without motor signs. The pupils may be equal, or one may be larger than the other. The blood will show an increase in the number of leukocytes. The spinal fluid may be turbid, and will show an increased cell-count, with probably the gold-curve in the meningeal zone. As the pus accumulates, we will have pressure symptoms; the temperature is lower; the pulse-rate falls; the stupor and mental hebetude increase, and the cortical irritation symptoms give way to pressure signs and paralysis. This combination of general symptoms denoting an infection, plus rapidly increasing focal symptoms, following a scalp wound or a fracture, presents a clinical picture which cannot be mistaken.

**DEEP OR LATENT ABSCESES.**—The symptoms of subcortical brain abscesses vary. The etiology may so affect the symptomatology as to produce a different picture for traumatic or otitic abscesses.

The deep subcortical latent abscesses call for the greatest skill in diagnosis.

The consideration of the symptoms of brain abscess is rendered easier by dividing them into three groups: (1) symptoms due to deep-seated suppuration; (2) symptoms due to increased intracranial pressure; (3) focal symptoms.

1. *Symptoms Due to Deep-seated Suppuration.*—If there is an absence of pus in other parts of the body and there is no other cause, the occurrence of fever with other signs of sepsis may aid us to form a diagnosis. Fever and the attendant signs of sepsis, viz., general malaise, loss of appetite, headache, occur in remissions and exacerbations. This variation is dependent upon the successive increase in size of the abscess and is characteristic. The fever in the latent or preactive stage is rarely over 101° F. (38.3° C.), usually from 99°-100° F. (37.2°-37.8° C.), although in the acute period of active manifestation it reaches a higher mark. Slight chilliness with a rise of fever occurs usually at night. The patients frequently look sickly, pale, jaundiced and emaciated.

Typical chills may occur in abscess, but repeated chills are rather indicative of septic sinus thrombosis. A high continuous fever speaks rather against abscess and for purulent leptomeningitis, sinus thrombosis or extradural pus. The presence of fever in suppurating middle ear or mastoid disease is no indication of abscess.

The temperature may be normal for a long time during the latent period, and Macewen first called attention to the frequency of subnormal temperature. In the period of acute manifestation, the headache is extremely violent and constant. During the latent period it is intermittent. Characteristic of the headache is its regular increase during the evening fever. This headache may be absent during the rest of the day, and is increased by anything that increases the intracranial pressure.

In otitic abscesses, and in others also, the pain may be localized over the abscess, and is much increased by percussion. This localized tenderness does not appear when there is inflammation of the mastoid or the neighboring temporal bone in middle ear trouble. In many cases this circumscribed localized pain and tenderness is very valuable in the localizing of abscesses.

Vomiting is important and is present in the majority of cases, especially cerebellar cases. Mere change of position, from reclining to sitting, may bring on vomiting. Vertigo is of little value.

2. *Symptoms Due to Increased Intracranial Pressure.*—The condition of the sensorium varies with the amount of intracranial pressure in the latent stage. There may be very little intracranial pressure for the reason that, unlike brain tumor, abscesses do not compress the brain tissue, but liquefy, destroy and replace it; and therefore large abscesses in a quiescent stage, even to the size of a duck's egg in the frontal lobe, may produce no disturbance of intelligence or of consciousness. In the stage of activity however, and just before rupture, we have the typical mental hebetude, somnolence, often delirium and hallucinations.

A slow pulse of 60 or less is always indicative of increased cerebral pressure, other causes being absent; but a rapid pulse in the acute stage is often present, and is not a contra-indication to abscess. During any fever the pulse usually becomes somewhat more rapid, but in abscess there is often a decline of the pulse rate with increased somnolence during the evening rise of temperature; and this, if found, is a very valuable symptom. Optic neuritis is more frequent than in tumor, but not so well developed (as to degree). If optic neuritis is absent the abscess is either of very acute development or small in size; abscess of frontal lobe has most marked optic neuritis. Optic neuritis, however, owing to the absence of increased intracranial pressure, is usually absent during the latent period.

3. *Focal Symptoms.*—Focal symptoms help much to make the diagnosis, if the abscess is present in the psychomotor or frontal lobes. Focal signs in abscess may come and go because of the varying size of the abscess and the disappearance, temporarily at least, of the surround-

ing softening. We may have large abscesses of the centrum ovale without focal signs: for the pus at first separates the white fibers instead of destroying them; and if the gray matter is intact, a whole lobe—Bergman says the greater part of a hemisphere—may be destroyed, without the development of a focal sign. The closer, however, the abscess is to gray matter and the greater destruction of tissue, the more focal signs are developed. As in brain tumor, we must distinguish between focal signs due to destruction and focal signs due to pressure from edematous infiltration. The latter may come and go; the former are permanent and localizing. As abscesses may be present in any part of the brain, we may have any of the corresponding focal signs.

Traumatic abscesses of *psychomotor area* are characterized by the rapidity with which monoplegia and hemiplegia follow the jacksonian epilepsy; or, if the abscess is deep-seated, the rapid, but not apoplectic, development of a hemiplegia without hemianesthesia. The paralysis is rarely complete.

Abscess of the *right frontal lobe*, like tumors in this region, may have no specially localizing signs: on left side, when large, we may have motor aphasia, involvement of right facial, even of arm; we may also have the typical symptoms of left frontal lesions. (*See chapter on Brain Tumor.*)

The *hearing center* is of value only if opposite ear has not been the seat of previous inflammation. Hence, according to Barr, it is of no value in two-thirds of the cases, because the purulent otitis is often bilateral.

Sensory aphasia is present in abscess of the *left temporosphenoidal lobe*. It may become manifest only a few days before the acute stage of the abscess sets in, and is at times associated with alexia. It is very important to remember that in most cases the sensory aphasia is transitory and not permanent; this is due to the fact that the abscess is usually on the underside of the temporosphenoidal lobe, which lies above the roof of middle ear, and affects the speech center only by distal pressure. Even epidural abscesses may affect the speech center by pressure.

Latent abscesses of the *right temporosphenoidal* are differentiated with difficulty from tumors, because fever is so frequently absent. We must rely then on the etiology. Bergman says that even with all our diagnostic aids we frequently make mistakes in temporal abscesses.

*Cerebellar Abscess.*—With the abscess in the lateral lobes we will usually miss marked cerebellar signs, unless the pressure of the abscess affects the *vermiform lobe*, when we will have marked ataxia. Then the centers and roots of six of the cranial nerves may be affected, but not so often as in tumor. Vertigo may just as well be due to labyrinthine as to cerebellar trouble, and is therefore of little value. Vertigo, uncertain gait, and retraction or stiffness of the neck are fairly often associated in cerebellar abscess. We can see, therefore, that the diagnosis of cerebellar abscess has usually been made after the mastoid has been opened. In 19 operated cases tabulated by Koch, the abscess was found

in 8 cases by the discovery of a sinus leading to the abscess during mastoid operations; in 7 cases, by aspirating in all directions and finally finding the abscess in the cerebellum; and only in 4 cases was the diagnosis properly made before the operation by a consideration of signs and symptoms.

**COURSE OF DISEASE.**—Chronologically the above symptoms of latent brain abscess can be divided into four periods: (1) the initial stage; (2) the latent stage; (3) the stage of manifest disease; (4) the terminal stage.

The primary stage corresponds to the etiological factors, the trauma, or the sinus or ear disease. The secondary or latent period may be of only a few weeks or months duration, or it may last for years. During this period the symptoms are undetermined, and the presence of an abscess is rarely suspected unless it can be connected up directly with the cause. The symptoms are rarely interpreted correctly. The occasional headaches are overlooked. The periodic rises of temperature are attributed to other causes. The epileptiform convulsions, when they occur, are looked upon as real epilepsy. However, the progressive emaciation and loss of strength, the general apathy and mental depression and periodic attacks of passing mental confusion should put us on our guard and make us suspect the presence of an abscess.

The signs of manifest abscess are usually very sudden in the onset, marked by violent delirium and very stormy and short in duration. Unless surgical intervention is prompt, they pass quickly into the terminal stage, which is usually an acute purulent leptomeningitis.

Rupture into the lateral ventricle causes convulsions, delirium, rapid coma, tetanic contractions of the extremities with bilateral ankle clonus and bilateral Babinski's sign, chills, high temperature, Cheyne-Stokes respiration, and death in a few hours.

**Diagnosis.**—**SUPERFICIAL ABSCESES.**—The only mistake possible is to confuse a cortical abscess with a localized meningo-encephalitis of a non-traumatic character. In the former only do we have the history of an injury. Meningo-encephalitis is usually encountered during epidemics. It occurs during the course of the acute infectious diseases, especially grippe, and the focal signs occur simultaneously with the general signs, or at least, in encephalitis, they develop earlier than they do in the traumatic surface abscesses.

**DEEP OR LATENT ABSCESES.**—The diagnosis of brain abscess presents two great difficulties: first, in determining whether or not an abscess is present; second, in locating the abscess.

These difficulties are entirely out of proportion to the difficulty found in diagnosis of other brain lesions, viz., tumors and cysts. The signs and symptoms of brain abscess in the latent period, when surgical intervention offers the greatest hope, are not only obscure and indefinite but for a considerable period may be absent altogether. The great problem, therefore, is to be able to diagnose the presence and, if possible, locate the abscess in its latent period, or at least in the very early period of positive manifestation.

Given a certain group of signs and symptoms which lead one to suspect the presence of a brain abscess, the first point is the tracing of the source of infection. Bergman says that without the *Streptococcus pyogenes aureus* there cannot be a brain abscess. If this is correct, then we should at least be able to find the source of infection. Now this is notoriously difficult. Pus-forming organisms always come from without; this is the most important and the first point. With the development of bacteriology, the theory of idiopathic abscesses has collapsed.

*Subdural Hemorrhage.*—Here the interval of time is an important factor. Hemorrhages occur more often after an interval of hours, rather than days and weeks, after an accident. The course is more rapid, and the symptoms and signs reach their height in a few hours or in a day; whereas, in superficial cortical abscesses, a longer period of time is required. Delirium, fever, chills and other signs of pus-infection are absent in subdural hemorrhages.

In the latent period, all wasting diseases which are attended with periodic attacks of fever, headache and progressive emaciation must be excluded. After this has been done, the diagnosis must be made between brain abscess and brain tumor. As a rule, in tumor, all of the signs of increased intracranial pressure are more marked than in abscess. During the period of latency, a choked disk would speak for brain tumor rather than for abscess. If the coincidence of periodic headaches with irregular, periodic rises of temperature can be ascertained, the fact would speak for abscess. The more clearly defined all the general and focal symptoms are, the more does it tend toward tumor. The more obscure and ill-defined, the more the symptoms would speak for an abscess.

Slow progressive development of signs and symptoms would speak for a tumor; rapid development, fever, chill and delirium would speak for an abscess in the manifest stage.

*Traumatic Neurosis.*—Great care must be exercised in cases of traumatic neurosis not to make a tentative diagnosis of brain abscess. It should never be done except in the presence of the manifest symptoms: viz., chill, fever, delirium, and undoubted sign of focal lesions based upon the presence of organic signs and symptoms which must be carefully differentiated from functional signs and symptoms, so common in traumatic neurasthenia and hysteria.

Middle-ear suppuration and mastoid disease in children are very often associated with localized *serous meningitis* (meningitis sympathetica), which can produce signs of local superficial abscesses. These cases of meningitis sympathetica at times show violent localized headaches and tenderness over the skull, inequality of the pupils, paresis of the sixth and seventh nerves. After a perforation of the ear drum or mastoid operation, all these symptoms disappear. It has been shown, however, especially by Strauss in connection with suppuration of the thymoid, that these so-called cases of sympathetic meningitis are true cases of meningitis with increased leukocytosis of the cerebrospinal fluid, and, unless relieved, at times terminate in cases of acute leptomeningitis.



*Otitic Sinus Thrombosis.*—In typical cases of septic sinus thrombosis we have the general signs of pyemia with periodic chills, high temperature, quick rise and fall of the temperature. In atypical cases the differential diagnosis cannot be made, except that focal signs will speak for abscess.

In order to emphasize the *difficulty of diagnosis in latent abscesses*, let us introduce Oppenheim's experience. He says that in the majority of cases of suspected abscess he could rule out abscess at once without any trouble. In 35 cases he had serious difficulties in diagnosis. In 14 of the 35 cases he made the diagnosis of abscess. The other 21 cases were either localized meningitis, cerebrospinal meningitis, encephalitis, otitis media or brain concussion.

Of the 14 abscesses, 4 belong to the period antedating the days of brain operations. In 5 cases an operation was deemed inadvisable, either because the abscess could not be located or because of complications. In 5 cases an operation was performed, in 2 of these the abscess was not found, although present. In the 3 remaining cases the operation was successful, but only 1 case recovered, the other 2 dying of the complicating meningitis.

**Treatment.**—**SUPERFICIAL ABSCESSES.**—The region of the original wound usually corresponds to the area of the surface involved. In case of doubt the surgeon should be guided in his choice of location of the operation by the focal signs which are present.

**DEEP OR LATENT ABSCESSES.**—*Prophylactic treatment* should be directed in *traumatic cases* to **proper surgical treatment of the initial wound**. **Strict antisepsis** should be employed for scalp wounds. When in doubt, the **x-ray** should be utilized for the purpose of detecting depressed and comminuted fractures of the skull, especially under the temporal muscles. *Stab wounds* with perforation of the skull should be **trephined**.

*Middle-ear suppuration* should have careful attention. All obstructions to the outflow of pus should be removed. Nasal obstructions which prevent a free discharge from the ethmoid cells or frontal sinuses should be removed. Mastoid suppuration should be subjected to radical operation. When the abscess is located it should be evacuated at once. Death occurs frequently without rupture, as a result of general edema of the brain, the general symptoms being followed by coma and death. This is especially true of abscesses of the cerebellum, and at times is associated with an internal hydrocephalus.

**Prognosis.**—**SUPERFICIAL ABSCESSES.**—The prognosis of surface abscesses is very good, if the surgical interference is timely and prompt.

**DEEP OR LATENT ABSCESSES.**—The prognosis varies according to the cause and location. We may say that practically no cases recover without surgical intervention. A few cases of spontaneous absorption of small abscesses have been recorded. There are also cases of spontaneous cure recorded, in which the abscess burrowed through the neighboring bony tissue into one of the cranial sinuses. The rule is that a fatal

mination occurs either by rupture through the cortex or into the ventricles, unless the abscess can be evacuated. Traumatic and otitic abscesses are most favorable as to prognosis.

## 2. ABSCESSSES DUE TO PURULENT INFLAMMATIONS OF THE BONE

*Middle-ear suppuration and mastoid abscess* are present either in the temporal lobe or in the cerebellum.

The most important contribution concerning brain abscesses in middle-ear trouble has been given to us by Körner. He proved that we could accurately locate the seat of the abscess in the brain if we knew which part of the temporal bone was diseased. Körner made autopsies on 109 cases of otitic brain abscess: 86 times the temporal bone was diseased to the dura mater, 8 times half way through the bone, and in only 15 cases was it healthy. In 40 abscesses, 38 times the seat of abscess was immediately below the diseased bone, and the dura was involved. The dura was frequently adherent to brain and diseased bone.

If the roof of the middle ear is diseased, the abscess is in the temporal lobe. If the mastoid cells or the posterior portion of the petrous portion of temporal lobe is the seat of inflammation, the abscess is in the cerebellum; the middle lobe of cerebellum is involved, if this purulent inflammation passes through the semicircular canals. Bergman speaks strongly in favor of the above method of localization.

Another point in diagnosis is, that *otitic suppuration* when associated with a *cholesteatoma*, whether the latter be primary or secondary, is more apt to cause abscess of the brain than an uncomplicated one. The reason for this is given by Kirehner. The cholesteatoma penetrates the bone; in its growth it ramifies the haversian canals for a considerable distance around its base; makes the bone thin and friable, fills it with large cavities, and in this way renders the invasion of the pia an easy matter and paves the way for an abscess. In addition to this, the pus is dammed back by the cholesteatoma, and the breaking through and the corrosion becomes an easily accomplished fact. In these cases the pus is decomposed and cholesteatomatous masses float in and on it. Virchow, in 60 cases of otitic brain abscess, found one-fourth with cholesteatoma. Two other factors predispose to the formation of otitic brain abscesses: (a) the course of suppuration in acute or subacute exacerbations, the pus being fetid; (b) the presence of large granulation masses on the middle ear, or deep in the external ear, the granulation masses acting as a dam to the pus. Thus, important diagnostic data can be obtained from the examination of the external ear. Another important diagnostic point in otitic abscesses is the fact, brought out by Körner, that otitic abscesses are oftener on the right side than the left. Herzberg showed that the transverse sinus on the right side lies deeper in the bone than on the left. Körner proved this to be the case in 70 per

cent. of his autopsies. This causes the bone, therefore, to be thinner and more easily perforated by a cholesteatoma or by the suppurating process.

When the origin of the abscess is in the *roof or attic of the middle ear*, the bone having become inflamed or corroded, the first step is a purulent pachymeningitis, and this is followed either by an extra- or intradural abscess. The intradural abscess is at first connected with the dura mater, afterward becomes separated by becoming encapsulated, and then becomes subcortical in the temporal lobe. Often we have both extradural and intradural brain abscesses at the same time; this is very important to remember (E. Hoffmann). We can diagnose an epidural or extradural abscess (Bergman) only by the following signs: by external signs when the pus escapes either through the middle ear, through temporal bone, or mastoid cells. Abundant flow of pus, of short duration, will arouse suspicion of abscess, especially if the signs of previous increased intracranial pressure disappear with the flow of pus. Discharging fistulae and especially edema, or a fluctuating abscess over the mastoid bone, lead to diagnosis of an epidural abscess of the middle or temporal fossa.

The difficulty of locating an otitic abscess is increased by the fact that middle-ear suppuration is often associated with *suppuration of the mastoid process*. Then we must look for caries or otitis, because, if the latter process is either in the antrum or in the mastoid, it is liable to determine the seat of abscess.

A badly located or a small tympanic perforation is apt to cause brain abscess by damming back the pus. Otitic abscesses have an imperceptible and unknown (as to time) beginning; are never sudden. trauma plays no rôle.

Otitic cerebellar abscesses are very difficult to diagnose, and are frequently complicated with sinus thrombosis and leptomeningitis and masked by the latter. We look for cerebellar abscesses in caries of the sigmoid fossa, of the sulcus transversus, of the labyrinth and the mastoid cells (Koch). Koch has proven that cerebellar abscesses before the age of ten are rare (2 out of 105). Hence, prior to this age we must look for temporosphenoidal abscesses.

*Rhinogenic abscesses* are due to purulent processes in the upper nasal passages and the sinuses connected with them, viz.: the frontal, sphenoidal and maxillary. The route which the pus may travel is through the cribriform plate, along the horizontal plate of the ethmoid, or through the orbital cavity along the optic nerve. Simple operations, like the removal of polypi or of adenoid vegetations of the nasopharyngeal plate may, if followed by infection, cause cerebral abscesses. Just as in otitic abscesses, the inflammation and caries of bone of the above-named cavities cause extradural and intradural abscesses and leptomeningitis, with an associated phlebitis of the sinus cavernosus, the difference being in the greater frequency with which they are associated in the same case. The course of the inflammation from the molar sinus is through the orbit by the way of the orbital veins. Out of 20 abscesses of the brain

to the above source of origin, 19 were found in the frontal lobe and only one in the temporal.

This great frequency of *abscesses of the frontal lobe*, following the above-named diseases, makes the diagnosis easy, when the general signs and symptoms of abscess are present. The localization is made from the seat of the pus infection, but, like tumors of the frontal lobes, the general and special signs may be absent. In a case on record in the Cincinnati Hospital, the boy was in the wards fully sixty days for frontal sinus disease; he was up and about daily and was considered bright, active and intelligent. Two days before death, he suddenly developed the general signs of a brain abscess; the operation revealed an abscess of the size of a duck's egg, discharging foul, offensive pus, which must have been present for months.

### 3. TUBERCULOUS ABSCESES

In connection with tuberculous abscesses two things are positive: one is that after the formation of a tubercle in the brain, a purulent inflammation may occur around the tubercle, which, as in reported cases, may completely break down, a microscopical examination being necessary to determine its tuberculous origin; and, secondly, Koch has shown that the cause of the purulent inflammation may be the dead tubercle bacillus. These tuberculous abscesses are of special interest in one direction: namely, that we may have all the indications of a cerebral abscess without any known traumatic or purulent cause, and still be justified in the diagnosis and the operation.

The difficulty in the diagnosis of tuberculous abscesses is twofold. In the first place, there is an absence of all known causative factors in the case as it lies before us; and, in the second place, the general symptoms of tuberculosis overlap those of the brain trouble, and distort the clinical picture. These abscesses are very frequently in the cerebellum, and then by producing basilar symptoms, simulate very closely either a tuberculous or syphilitic meningitis.

### 4. METASTATIC ABSCESES

Metastatic abscesses (Fig. 3) are generally pyemic in origin, multiple, and usually not good subjects for diagnostic skill. Bergman says, however, that at times they are solitary and operable. Macewen says that solitary metastatic abscesses constitute one-third of the pyemic abscesses; and Martin found, in 22 cases, 9 of pyemic metastatic abscesses of the brain. The origin of these metastatic brain abscesses is usually the lung, viz., gangrene, abscess, empyema, pleurisy or bronchiectasis, but they may be secondary to pus foci in any part of the body. Like most brain lesions of embolic origin, the metastatic abscess, if solitary, is usually found in the left carotid region (Martin's 7 cases out of 9).

## 5. SO-CALLED IDIOPATHIC ABSCESSES

To Bergman's classification of abscesses, a fifth group should be added: namely, the group, not so much of idiopathic abscesses, but of abscesses in which there has been no previous deposit of pus in the body from which the streptococci could be drawn. This leads us to the discussion of so-called idiopathic abscesses. That there can be no idiopathic abscess in the sense of an absence of some cause for suppuration we must admit. But we know that we can have primary brain abscess which

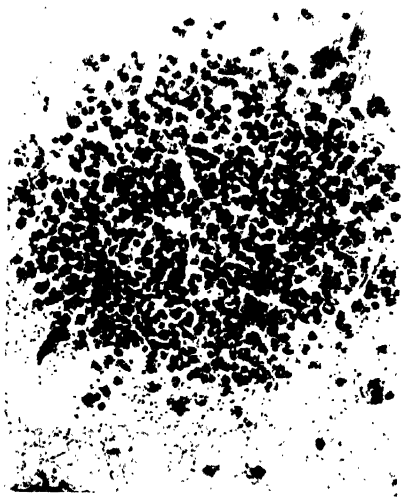


FIG. 3.—MILIARY ABSCESS OF THE BRAIN.

cannot be grouped under any of the preceding heads. This is an exceedingly important point to remember when one is confronted with the necessity of making a diagnosis or differential diagnosis. Martin has worked up this subject and points out four cases of Strümpell's observed during an epidemic of cerebrospinal meningitis in which no other cause could be found. Oppenheim says that there is no doubt whatever that the influenza bacillus not only can cause a meningitis or an encephalitis, but that also an abscess may complicate the meningo-encephalitis, the latter may disappear and the former may remain behind or the abscess may occur independently of a meningo-encephalitis. He also reports cases in two articles in which he calls attention to the fact that acute non-purulent cortical encephalitis may simulate brain abscess.

Latent abscesses may break through the gray cortex covering the

and cause a general leptomeningitis purulenta, or they may cause rapid exitus by breaking through the walls of the lateral ventricles.

In other cases the abscess may cause a thrombophlebitis or a sinus thrombosis, and secondarily a general pyemia.

Cerebellar abscesses, by pressure upon the canal of Sylvius, may be complicated by an internal hydrocephalus.

In very rare instances an abscess may be absorbed, leaving a scar.



## CHAPTER VIII

### BRAIN TUMORS

By H. H. HOPPE, A.M., M.D.

Introduction, p. 631—Etiology, p. 631—Frequency, p. 632—Pathology, p. 633—Symptomatology, p. 644—General symptoms, p. 644—Localizing signs, p. 650—Brain-tumor symptom-complex with termination in recovery: pseudo-brain tumor, p. 686—Course and duration, p. 693—Diagnosis, p. 693—Differential diagnosis, p. 693—The x-ray as an aid in diagnosis, p. 697—Treatment, p. 698—Medical, p. 698—Surgical, p. 698—Prognosis, p. 705.

**Introduction.**—The researches of both clinicians and pathologists in the field of brain tumors have been so fruitful of results in the past few decades that, theoretically and in the abstract, the subject may be considered almost a closed book. The researches of Cushing in the field of pituitary tumors and of others in the field of tumors of the pineal gland have even enriched our knowledge of the function and innervation of the chain of endocrine glands. The function of the cerebellum has become more clear also through these investigations and the indications for surgical intervention have been put on a more accurate basis.

The clinical and pathological investigation of the localization of brain tumors has more than anything else increased our knowledge of the physiology of the brain, which has thus in turn rendered the diagnosis and localization of brain tumors more accurate.

Notwithstanding all this, the diagnosis of brain tumor is relatively infrequent. In reality, however, brain tumors are far more common than the records of the surgical and pathological annals would indicate; for many cases remain undiagnosed. A wider interest and the early recognition of the symptoms would tend, not only to increase the number of cases recognized, but would ameliorate the ultimate symptoms by timely radical or remedial surgical intervention. That tumors are frequently overlooked is proven by Blackburn,<sup>1</sup> who found 29 tumors of the brain in 1,642 autopsies in the Government Insane Asylum, only 2 or 3 of which were diagnosed during life. Oppenheim<sup>2</sup> states that the brain is the seat of predilections of tumors, and Bruns<sup>3</sup> maintains that at least one-half of the tumors of the brain are overlooked.

**Etiology.**—We cannot enter into the discussion of the pathological or biological causes of tumors as such.

**SPECIFIC ORGANISM.**—Some tumors are caused by a specific organism. The tubercle and the gumma are illustrations of this kind. The cysticerci and echinococci are very rare in America. In a very large ex-



perience, the author has never seen a case. The glioma is the special tumor of the brain and the sarcoma of the membranes. Children usually develop tubercles, but frequently also gliomata; whereas in the adult, tubercles are rare. In 29 cases Blackburn has seen but one tubercle, whereas, tuberculosis is very common in insane asylums.

**TRAUMA.**—To-day, in view of the wide spread of accident insurance and the adoption of compulsory insurance in most states, *trauma* as a cause of brain tumor assumes a very important position. There can be no doubt that a trauma to the head, sufficiently severe to produce fracture or concussion, can be the immediate and direct cause of tubercles and of gummata, by creating a favorable soil for the development of these two growths, namely, bruised brain tissue. In every such case, however, there should be a chronological relation between the accident and the gradual onset of the symptoms, culminating in the complete symptom-complex of brain tumor.

We have also seen a cyst, the size of a cherry, develop in the substance of the left temporosphenoidal lobe as a result of a depressed fracture and the penetration of a sharp spicula of bone into the cortex. The fracture was overlooked because it was covered by the temporal muscle. There is hardly a scientific basis for a causal relation between trauma and other forms of brain tumor, especially when we consider the enormous frequency of concussion of the brain with or without fracture and the relative infrequency of brain tumors. There is reason, therefore, for great caution in expressing an opinion on the cause of a given brain tumor. Cushing<sup>4</sup> argues that when tumor symptoms follow immediately upon a trauma, the latter serves only "to bring into the open the symptoms of a previously obscure growth." This is caused by the rupture of a blood-vessel in a vascular glioma or by concussion edema. This observation was also made by Starr,<sup>5</sup> and confirmed by two autopsies.

**SEX.**—As to sex, Cushing, Bruns, Gowers, all agree that males are affected twice as often as females. Brain tumors are infrequent in infants and after 60 years of age. They occur most frequently in the third and fourth decade of life. In Starr's<sup>6</sup> table of 600 cases, 300 occurred in children below the age of 18, and 300 after this age. In Cushing's 130 cases, 22 occurred in the first decade, 13 in the second, 28 in the third, 37 in the fourth, 20 in the fifth, 8 in the sixth, and 2 in the seventh decade. Tooth's<sup>7</sup> tables, based upon 500 cases, give 23.6 per cent. as occurring in the third decade and 29 per cent. in the fourth and 17 per cent. in the fifth decade.

Tumors of the pineal gland are more frequently found in children than in adults, and they then cause the typical symptom-complex.

**Frequency.**—Cushing states that among 3,150 autopsies held in the Johns Hopkins Hospital, 55 were cases of brain tumor (1.7 per cent. Other statistics place the percentage even as low as 0.8 per cent. The number of brain tumor cases admitted to the Cincinnati General Hospital is less than one-half of one per cent. Cushing's statistics Johns Hopkins are not of much value, because of the fact that

cases received at this hospital are not of the same character as those of a general hospital, such as the Cincinnati General Hospital. In a large private practice limited to nervous diseases the writer sees about 5 new cases of brain tumor per year. Still this number, as seen in private practice, approximates very closely Cushing's figures of Johns Hopkins Hospital, viz., 1 to 250 admissions.

Bruns states that 2 per cent. of all neurological cases are brain tumors. This figure is undoubtedly too high.

**Pathology.**—We cannot go into the subject of the cellular pathology of brain tumors in detail. All tumors found elsewhere are found in the brain and, in addition, the brain has its own special tumors. Glioma

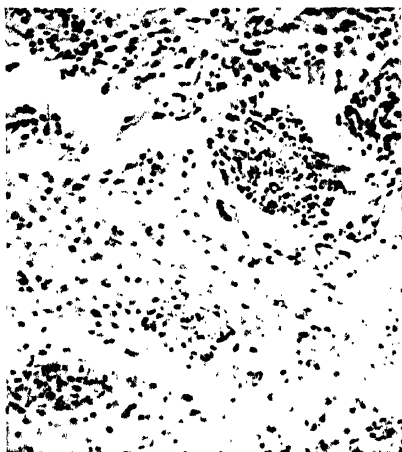


FIG. 1.—CELLULAR STRUCTURE OF GLIOMA OF THE BRAIN.

and sarcoma are most common and, according to Starr's tables, are twice as frequent in adults as in children. Gummata are next most frequent in adults and very rare in children. The solitary tubercles are found more frequently in children than in adults; in fact, they are very rare in adults. Cysts are more common in young children. Carcinomata, fibromata, osteomata, psammomata, cholesteomata, adenomata, angiomas and echinococcus cysts are among the rarities.

**GLIOMA.**—Glioma is the typical brain tumor, because it has its origin from the interstitial tissue of the nervous system, namely, the neuroglia (Virchow). Mallory and Stroeck<sup>8</sup> have shown that gliomata may also arise from the ependyma. The glioma develops from embryonic cells and, varying with the rapidity of the growth, the cellular structure of the tumor may be chiefly round-celled or may approach more the mature stage of development of the glia tissue and hence the hybrid tumor of former days (gliosarcoma?).

The gliosarcoma is no longer recognized as a special tumor because of the fact that gliomatous tissue is derived from the ectoderm, whereas sarcomata are of mesodermal origin. Cushing subjected 69 cases of brain tumor to a very careful anatomical and histological study and found that 44—namely, 66 per cent.—were gliomata. He states that only one sarcoma was found and that many of the 44 histologically proven as gliomata would in former years have been classified as gliosarcomata. Frederick B. Clarke,<sup>9</sup> in a study of 99 cases of brain tumor, classifies them as follows: gliomata and ependomata, 38 (about 38 per cent.); hemangioperitheliomata and peritheliomata, 37 per cent.; metastatic carcinomata, 7; gummata, 6; tuberculomata, 5; sarcomata, 4;



FIG. 2.—GLIOMA OF THE FRONTAL LOBE.

gliosarcomata, 1; blood-cysts, 1. Tooth,<sup>10</sup> out of 258 cases, in which the pathology was verified, gives the following percentages: glioma, 49 per cent.; fibroma, 5 per cent.; endothelioma, 14 per cent.; sarcoma, 8 per cent.; carcinoma, 5.8 per cent.; tuberculoma, 5.4 per cent. Starr,<sup>11</sup> however, still adheres to gliosarcoma as a distinct class, and places glioma as third in frequency, tubercles coming first in his tables and sarcomata second. In the cerebellum, Weisenberg<sup>12</sup> states that sarcomata occur about as frequently as gliomata.

If the growth of the glioma is very rapid, the cells undergo a fatty degeneration and liquefaction; hence the development of cysts and the yellowish color of the tumor in spots. These rapidly growing gliomata invariably infiltrate the brain tissue, and no line of demarcation can be found either macroscopically or microscopically. When the growth is of a slow nature the cells and fibrous elements are more mature, the growth is more firm and can, at least at autopsy, be shelled out, although



FIG. 3.—GLIOMA IN THE MIDBRAIN WITH INVOLVEMENT OF THE BASAL GANGLIA.

microscopically the cell infiltration extends beyond this visual margin of the tumor.

These tumors usually grow subcortically, and may be found in the



FIG. 4.—GLIOMA IN THE OCCIPITAL LOBE.

neocortex, cerebellum or brain stem. They may be as small as a hazelnut; they may occupy an entire half of the brain from the frontal to the occipital lobe, inclusive of the basal ganglia (*see* Figs. 2, 3 and 4). They may be of the consistency of the brain tissue itself and at the

operation, if very large, are apt to be easily overlooked. When the brain is hardened they frequently have a mottled appearance, reddish-yellow spots or streaks running through the tumor. At times a sudden large hemorrhage may take place into tumors of rapid growth, destroying them and leaving only the margins intact. Other tumors undergo a cystic degeneration either in spots or in the whole tumor, and everything, except the outer margin, may break down. These cavities are at times lined by epithelium and may be mistaken for true cysts.

W. T. Councilman<sup>13</sup> calls attention to the following peculiarities of gliomata: (1) the manner of growth is by infiltration, not expansion; (2) the glioma replaces tissue and the form of the tissue replaced may be perfectly preserved; (3) the cyst formation in gliomata is due not to degeneration but to fluid absorption of the tissue, and represents an accentuation of a condition common to the entire tumor; (4) the gliomatous growth is always limited to the tissue (neuroglia) in which it originates, and never infiltrates the membranes; (5) gliomata never give rise to metastases; (6) gliomatous and sarcomatous tissue may grow side by side in the same tumor, but Councilman has seen it only once in 25 tumors which he studied.

When gliomata are located in the basal ganglia, close to the walls of the lateral ventricles, they may cause internal hydrocephalus, which may come and go, and tend to obscure the clinical picture of the disease.

**SARCOMA.**—Sarcomata may be primary. At times they are metastatic and multiple. Sometimes secondary, multiple, hemorrhagic, cystic sarcomata are found. We have encountered one perforating sarcoma of the occipital region, causing autotrepation with a fluctuating mass under the scalp. The tumor itself compressed both lobes, causing blindness. The benign character was proven by the complete recovery of sight which followed its removal.

The primary sarcomata are of interest because they offer the best prospect for surgical relief. They grow from the membranes of the brain, periosteum or even the bone itself, and compress the brain substance rather than infiltrate and destroy it; they can therefore be radically removed with intact brain substance. Royce<sup>14</sup> holds that sarcomata originate at times from the brain itself, viz., in the pituitary substance, in the walls of the vessels, and in the sheaths of the nerves. Sarcomata, especially, make an early diagnosis desirable, for the earlier the diagnosis, the smaller the growth and the less damage to the brain. Sarcomata are found both in the cerebrum and in the cerebellum. They are slow in growth, do not often undergo degeneration, although cyst formation has at times been encountered, as well as areas of fatty degeneration. Growths usually classified as sarcomata Cushing calls endotheliomata. Most endotheliomata and sarcomata are benign, and readily removed, because they do not infiltrate the brain tissue. Melanosarcoma is rare and always secondary. Multiple diffuse sarcomatosis is a rare condition. It may occur in the form of multiple small tumors, scattered over the membranes of the brain, more especially the posterior tables, or it may occur in the form of a diffuse infiltration of the membranes.

with the sarcomatous mass, without involving the brain tissue itself. This condition is exceedingly difficult to diagnose, and surgical operations are contra-indicated, because of the impossibility of cure.

**TUBERCLES.**—Tubercles of the brain are never primary, although the original focus may escape detection in children. They occur usually in children, and are rarely encountered in adults as presenting pure brain tumor syndromes. In Starr's tables they are four times more frequent in children than in adults. They occur with great frequency in the subtentorial region. When located in the region of the crura cerebri, of the corpora quadrigemina and the pons, they may cause a secondary



FIG. 5.—TUBERCLE FOUND BELOW THE MOTOR CORTEX.

It had undergone calcareous degeneration and become walled off by a cartilaginous membrane.

internal hydrocephalus which will tend to obscure the brain tumor syndrome.

Tubercles may be solitary or multiple. At times there is a localized, flat, diffuse infiltration of the meninges, meningo-encephalitis of tuberculous character, which may produce some of the signs of brain tumor (*see* chapter on Encephalitis).

Tubercles tend to undergo caseous degeneration and in rare instances may become walled off by a cartilaginous membrane and undergo a spontaneous cure. This probably took place in a case observed in the neurological wards of the Cincinnati General Hospital, in which a tumor was apparently latent for over 40 years (Fig. 5). The tumor was found below the motor cortex, surrounded by an area of recent softening, within being a dense cartilaginous mass surrounding a calcareous deposit. It was found in an individual who died at the age of 60 years and presented a history of a gradually developing hemiplegia at the

age of 18 years, which, however, disappeared completely after a year or two.

Tubercles grow from the membranes and are usually found on or near the surface. They infiltrate the brain tissue and are at times found below the cortex. In children these tubercles are often solitary; but we must remember in recommending surgical intervention that other growths may be in silent areas of the cortex, and also that there is always the possibility of a secondary tuberculous meningitis. In both adults and children tubercles, undiagnosed during life, are found on autopsy, usually in the cerebellum or in the so-called silent areas of the brain.



FIG. 6.—GUMMA OF THE CORTEX, GROWING FROM THE PIA MATER.  
Tumor turned back from its bed (postmortem).

**GUMMATA.**—Gummata are rare, the usual form of brain syphilis being the meningovascular exudate.

Gummata of solitary character, however, do occur, and may attain the size of an English walnut. They are not amenable to antisiphilic treatment. They are usually cortical, infiltrate the brain substance, and at times can be shelled out. Contrary to the teaching of a decade ago, they are objects of surgical procedure (Fig. 6). They have their origin in the vessels of the pia mater and may be found in any part of the brain.

A sharp line must be drawn between gummata and the exudative form of cerebrospinal syphilitic meningitis. The former is rare; the latter is perhaps one of the most frequent of all organic brain lesions. The former is amenable to surgical treatment and is not influenced by medical treatment; the latter is very successfully treated by antisiphilic treatment and should never be surgically treated.



FIG. 7.—FIBROMA OF THE ACOUSTIC NERVE IN THE CEREBELLOPONTINE ANGLE



FIG. 8.—FIBROMA OF THE HYPOPHYSIS.



**FIBROMATA.**—The fibroma is a connective tissue tumor, with few or no cellular elements, and occurs, with predilection, in the pituitary gland and is attached to the nerve trunks which leave the pons. The acoustic nerve is especially often the seat of these growths, giving rise to tumors of the cerebellopontine angle (Fig. 7).

A large fibroma (Fig. 8) about the size of a tangerine is shown here, growing from the pituitary gland.

Fibromata, in rare instances, may be multiple and may occur in the form of neurofibromata, attached to various cranial nerves (Recklinghausen's disease).

Bassoe and Nuzum<sup>15</sup> report a case of central and peripheral neurofibromatosis in which, aside from the peripheral fibromata, one was found in the cerebellopontine angle on both sides, another in the left gasserian ganglion, still another attached to the third nerve, besides numerous small ones attached to the roots of the spinal nerves.

**CARCINOMATA.**—Carcinomata are always secondary and may be multiple, occurring as metastases. They are very rapid in growth and always fatal.

**ADENOMATA.**—Adenomata occur in the hypophysis. Cushing says that primary epitheliomata may occur in the choroid plexus and are benign in character.

**CYSTS.**—Cysts may be primary or secondary. Primary cysts are those which arise from parasites such as cysticerci and echinococci, the latter being often multiple. Common in Germany and other central European countries, they are exceedingly rare in the United States. None were encountered in the pathological laboratory of the Cincinnati General Hospital. Traumatic cysts around penetrating spicules of bone are at times encountered, and may give rise to considerable destruction of brain tissue. Secondary cysts are found in connection with gliomata and at times with sarcomata. These are of surgical importance, because the mere tapping of the cyst will not be followed by a radical cure.

**Arachnoid Cysts.**—Localized encysted cerebrospinal fluid is frequently encountered both on the surface of the cerebellum and of the cerebrum. These accumulations are sometimes caused by very superficial and localized attacks of leptomeningitis serosa of unknown origin, or they are secondary to localized meningo-encephalitic attacks with cortical destruction, and are seen in conjunction with the underlying pathology of infantile cerebral palsy. Recent attempts to give surgical relief in the latter disease have exposed these localized collections of fluid.

**Other Cysts.**—Smaller cysts secondary to hemorrhage or embolic processes, gas cysts, which are always formed after death, have no clinical importance. Dermoid tumors and cysts are exceedingly rare. Cushing reports but one case in his very large experience.

**ANGIOMATA.**—Telangiectatic angiomata are occasionally found in operations for jacksonian epilepsy. They do not present definite pressure symptoms; and, although congenital, may not manifest cerebral pressure or irritation symptoms until in early adult life.

The writer has seen one case of angioma of the diploë of the skull with perforation of the inner table, the resulting extrusion, no larger than a cherry stone, causing a jacksonian epilepsy.

**PSAMMOMATA.**—True psammomata are found only in the pineal gland and occasionally in the choroid plexus. They, like cholesteatomata, are usually postmortem findings, and give rise to no clinical pictures.

**LIPOMATA, ENCHONDROMATA, and CHORDOMATA** are rarities.

**ANEURYSMS.**—Aneurysms are usually seen in connection with the basilar or vertebral arteries. Starr reports a case of traumatic aneurysm of the left internal carotid which presented all the signs of a brain tumor. Aneurysms are rarely diagnosed clinically, although they are not so rare on autopsy. Beadles,<sup>10</sup> in 1907, analyzed 555 cases of intracranial aneurysms.

The brain, when removed on autopsy, shows signs of general compression by a flattening of all convolutions. During life, after decompression operations, the most noticeable condition which confronts one is the bulging of the dura mater and the absence of normal pulsations. Spiller<sup>17</sup> has recently directed attention to an absolute increase in the size of the brain as one of the conditions found in brain tumor. Councilman<sup>13</sup> called attention recently to an increase in the neuroglia beyond the margin of the infiltration of the gliomata. Spiller and, recently, Clarke<sup>9</sup> have also attributed this actual increase in the size of the brain to a hyperplasia of the neuroglia, and state that it is not proportional to the size of the tumor. It may be moderate in large tumors and so marked in small tumors as to cause much enlargement of the hemisphere in which it is located. The overgrowth of the neuroglia is caused by pressure or by some substance elaborated by the tumor.

This hyperplasia of the neuroglia may occur in any kind of brain tumor. Spiller believes that this hyperplasia may occasionally be the cause of sudden death in brain tumor cases; the gradual increase of the intracranial pressure which it causes may interfere with the important functions of the medulla. It may likewise be the cause of impairment in mentality in some cases of brain tumor.

**INCREASED INTRACRANIAL PRESSURE.**—Increased intracranial pressure is found almost invariably in cases of brain tumor. It is greatest in tumors of rapid growth and in tumors so located as to dam up the fluid in the ventricles, thus causing an internal hydrocephalus. The increased intracranial pressure is due partly to the mechanical condition. In the normal state the cranial cavity is completely filled with the brain, its membranes and the cerebrospinal fluid. Any tumor which does not destroy an amount of brain tissue equal to its size will increase the content of the cranial cavity and therefore increase the pressure from within. Moreover, the cerebrospinal fluid is also increased in quantity probably—as is held by Frazier, de Schweinitz, Holloway—by the presence of an irritant toxin, and this in turn tends to vastly increase

already heightened intracranial pressure. We shall take this subject up more in detail when discussing the subject of papillo-edema in connection with the decompressive operation.

**CHOKED DISK.**—The cause and pathology of papillo-edema is of some importance, more especially since the decompressive operation has come into vogue. As a rule, we judge of the degree of intracranial pressure from the presence of and degree of swelling of the optic disk. There are two theories as to the genesis of papillo-edema: namely, the mechanical theory and the toxic theory.

No discussion of this subject is complete without taking into consideration the etiology of papillo-edema. Ever since Türk in 1846, and von Graefe, in 1853, called attention to the relation between intracranial disease and the occurrence of swelling of the papilla, the discussion has been undecided up to the present day as to whether the swelling is the result of a toxic condition plus inflammation, or whether it is merely and solely mechanical in its origin. Schmidt-Rimpler and Manz were the first to show, by laboratory experiments, that swelling of the disk could be caused by intracranial injections of fluid. If you hold with Leber, Deutschmann and the rest, that in tumors there is an irritant toxin in the brain which travels down the optic disk and produces an inflammation, you will naturally not advocate cerebral decompression for papillo-edema alone; if, on the other hand, you are an adherent of the mechanical theory, you naturally will advocate an operation.

There is this much to be said for those who hold the mechanical theory: First, Manz, Schmidt-Rimpler, Oppenheim, Schulten, Bramwell, Hoche, Merz and Cushing have been able to produce in the laboratory, by intracranial injections, all grades of papillo-edema, the degree varying with the degree of intracranial pressure. In the second place, a large number of men have observed the retrocession of the choked disk after palliative operations, among whom Cushing, Sängner, Axenfeld, von Bruns, Paton and others may be mentioned.

Even in the papillary swelling seen in nephritis, which is supposed to be typically of toxic origin, Cushing has shown that similar pictures are seen as in uncomplicated cases of brain tumor; and by operative interference, either by lumbar puncture or decompressive operation, he has demonstrated that the swelling is due to increased intracranial pressure, which will disappear if this pressure is relieved.

Those who hold the toxic inflammatory theory are supported by the authority of the physiological chemist, who tells us that there is some toxic element in all edema; and by the pathologist, who shows round-cell infiltration, new tissue formation, and cicatrization leading to atrophy. But Cushing holds that, in spite of all this, "it is the mechanical element producing edema which underlies these changes, and hence it demands mechanical therapy."

On the basis of his own laboratory experiments, by introducing both fluid and solid bodies into the cranial cavity, Cushing comes to the conclusion that "a simple increase of intracranial pressure without any inflammatory or toxic reaction is capable of producing a typical choked disk."

The mechanical theory is also supported by the observation of papillo-

edema in the new-born after difficult and prolonged labor, in post-operative cases where choked disk appears after brain operations for the removal of the gasserian ganglion, and after bursting fractures of the skull.

On the other hand, optic neuritis is not seen in meningitis until the symptoms caused by increased intracranial pressure set it up. Cushing calls attention to the fact that papillo-edema is never absent in meningitis when there is a complicating, obstructive internal hydrocephalus, and that he has observed the swelling to diminish and even disappear when the ventricle was punctured and emptied. He bases his views on the fact that in many of his two hundred cases of brain tumor he has been able to observe the papillo-edema develop, and that after numerous operations, both radical and decompressive, he has observed its recession. He holds that an unequal development of one side before the other, or on the nasal half before the temporal half, is no argument against the mechanical theory, but that it is due to the location of the tumor. Tumors growing in the hemispheres produce an edema in one papilla sooner, or at least more markedly, than in the other; whereas tumors of the cerebellopontine angle which compress the canal of Sylvius, thus giving rise to a sudden internal hydrocephalus, will produce a papillo-edema equal on both sides because of an equalized increased intracranial pressure.

It is not possible to reconcile these views of Cushing and others with the views of Frazier, de Schweinitz and Holloway, for the latter have come to a diametrically opposite conclusion with regard to the effect of increased intracranial pressure, and the consequent production of papillo-edema. The scope of this chapter will not permit the author to give any detailed account of their laboratory experiments. A few words will suffice. Frazier used two methods for increasing the intracranial pressure: one, the dry method, consisted of introducing a small rubber bag beneath the skull and dilating it to any desired size; and the other—the one he calls the wet method—consisted in injecting a normal saline solution into the cranial cavity, both tentorial and subtentorial. As a result of their experiments, Frazier, de Schweinitz and Holloway have come to the conclusion that increased intracranial pressure alone will not produce papillo-edema, but that one or more still unknown factors are at work in producing the results. de Schweinitz holds that he is satisfied that intracranial pressure is one of the elements in the causation of papillo-edema, but that he was never able to produce it in the living eye when a normal saline solution alone was used; also that if some irritant was added, like formaldehyd or iodin, a papillo-edema was produced. In this regard, Frazier holds that undoubtedly increased intracranial pressure is a factor, but he is inclined to doubt if it is the only factor, or even an essential one.

LOCAL CHANGES.—(a) *Local atrophic changes of the vault*, produced by direct pressure of the tumor, are very rare, although local convoluted atrophy of the inner table is sometimes seen in subcortical tumors.

(b) *Sellar Changes* (see Cushing hereafter on tumors of the hypophy-

sis).—Vascular abnormalities of the skull are observed in some cases in the form of an increase in the size of the diploetic sinuses or in the form of an abnormal grooving of the bone, caused by the dilatation of the vessels present or the formation of new vessels in the neighborhood of the growth. Heuer and Dandy state that this condition is more common in dural or cortical tumors of the cerebrum, especially in dural endotheliomata. This dilatation and increase in the number of vessels could be seen with the stereoscope and in at least one case led to a positive localizing diagnosis.

**Symptomatology.**—GENERAL SYMPTOMS.—Every brain tumor has its origin from a microscopic group of cells, and then grows more or less rapidly. It takes its origin either from within the brain substance or from the membranes, and encroaches upon some definite area having a fixed physiologic function, or it is in a silent area. The brain itself is practically incompressible, and the entire skull cavity is completely filled with the brain and the cerebrospinal fluid, which in turn is also incompressible. The tumor, as it grows from microscopic size, adds something to an already completely filled cavity; and, in the second place, it compresses, or destroys circumscribed areas in the brain, thereby interfering with its functioning. Two groups of symptoms result from these facts:

(1) Symptoms produced by general increased pressure, viz., pressure symptoms.

(2) Symptoms produced by compression, irritation and destruction of the circumscribed area occupied by the tumor, namely, focal symptoms. We diagnose the presence of a tumor by the general or compression symptoms; we localize it by the focal symptoms.

Theoretically speaking, the diagnosis and localization of brain tumors ought to be accurate and positive. There are to-day but few latent areas in the brain. Physiological and pathological researches have mapped out almost the entire cortical surface, the cerebellum and the brain-stem. The tracts, sensory, motor and association, are all charted, and we know much of the function of the gray matter of the thalamus opticus and the lenticular zone. Through Cushing's researches light has been thrown upon the symptom-complex of pituitary disease, and we have at least a presumptive knowledge of the pineal gland.

Practically, however, for various reasons, the diagnosis of brain tumor still offers great difficulty. The principal cause of this difficulty is the late stage in which the patient usually comes under observation: the absence of an adequate history of the previous symptoms; and the difficulty of getting autopsies in order to confirm the previous diagnosis. Often, too, the case presents itself, either with only the general symptoms, without focal manifestations, or there are only focal manifestations, and the general compression symptoms have not as yet had time to develop. At times the case is seen so late that both general and

local symptoms are masked by such a degree of clouding of consciousness that a diagnosis is impossible. In the majority of instances, however, both general and focal symptoms are present; they enable us to make a fairly accurate general and topographical diagnosis.

We must remember that tumors may develop in a silent area; that they may be slow in growth, infiltrating in character, and may present very few symptoms during life, consequently being found only on the autopsy table.

Cushing<sup>18</sup> divides the tumors of the brain into five clinical groups:

(1) Tumors which give absolutely no recognizable evidence of their existence, and are found postmortem.

(2) Tumors which present focal symptoms alone, with no evidence of a general increase in pressure.

(3) Tumors which give general symptoms alone, with no focal manifestations, when they happen to occupy a silent area.

(4) Tumors which give typical symptoms of general pressure with definite focal symptoms.

(5) The symptom-complex (general and local) of tumor, which, in the absence of a growth, is brought about most often by edema from one source or another. (Pseudo-Brain Tumors.)

Both the general and the focal symptoms of brain tumor are subject to two conditions: (1) the element of time; and (2) gradually increased compression of the brain as a whole and a gradually increased local destruction of tissues.

The general symptoms of a brain tumor must indicate that from a slight, almost imperceptible beginning, the symptoms of the patient gradually increase in severity and number, and that these symptoms are caused by a gradually increasing compression of the cranial contents.

Tumors, however, at times attain a certain growth, like tubercles or cysticerci, cease to grow, become calcified. The brain accommodates itself to and recovers from the pressure both local and general, and the individual lives for many years and dies of some other disease (see Fig. 5). Or a tumor may be located near the wall of the lateral ventricle (Figs. 9 and 10) and give rise to repeated attacks of internal hydrocephalus, thus obscuring the progressive development of the local and general symptoms.

In other very rare cases, however, the growth is so small, so insidious and slow in development, that no general symptoms at all are produced (Figs. 9 and 10).

On the whole, however, we may say that symptoms pointing to a *gradually* increasing and progressive compression of the cranial contents are very characteristic of a brain tumor, and such symptoms are usually present. These general symptoms are headache, vomiting, vertigo, choked disk, convulsions and mental symptoms, changes in pulse and respiration.

**Headache.**—The headache of brain tumor is characterized by its



FIG. 9.—TUMOR OF THE THALAMUS, EXTENDING SUBCORTICALLY IN REGION OF THE GYRUS ANGULARIS.

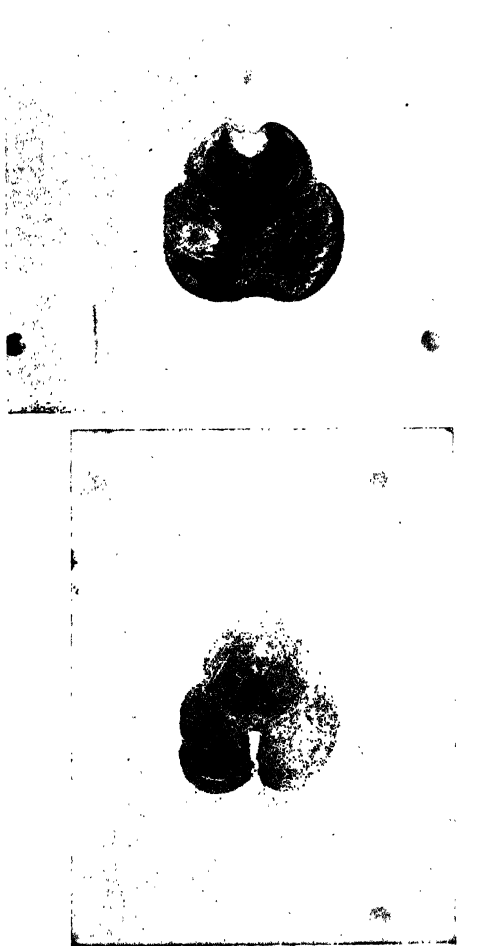
severity. It is general in character, and is usually not more severe in the region of the tumor. Frontal tumors may cause occipital pain and



FIG. 10.—SECONDARY INTERNAL HYDROCEPHALUS IN TUMOR.  
Same case as Figure 9.

subtentorial growths may have a predominance of frontal pain. The headaches may last for hours, even days, and are followed by more or less long periods of intermission. They are increased by anything which increases intracranial tension, heavy lifting, straining at stool,

coughing, sneezing, a jar to the head or body. It is usually described as a bursting, thumping headache, and is often relieved by vomiting.



**FIGS. 11 AND 12.—SMALL ROUND EPITHELIOMA OF PONS AND PEDUNCLE.**  
Serial sections of same brain stem.

During the headache the pulse is usually slower than normal. There is general apathy, and mental hebetude.



Sometimes the headache is so severe that it is accompanied by a more or less stuporous delirium, which in one case (Figs. 9 and 10) lasted for periods varying from three days to several weeks. This patient had four or five attacks of this kind, and in the intervals between attacks—which lasted for months—was well enough to play and go to school as usual. These exacerbations and remissions were explained on autopsy by the finding of an internal hydrocephalus which complicated the growth.

Headache is not an early symptom, because it is the product of pressure and tension of the dura mater. Small tumors and those growing in the interpeduncular space, where there is much erosion and destruction of the sella, or in the cerebellopontine angle, where there is some room for expansion at the expense of the cerebrospinal fluid, may produce no headaches at all or such headache may come on very late.

*Vomiting.*—Vomiting also is dependent upon greatly increased pressure. It usually occurs during an attack of headache. In subtentorial growths a change of position or even the turning of the head may bring it on. Only when intracranial tension is very high is vomiting projectile and unaccompanied by nausea and pallor; at other times the vomiting may be accompanied by retching, nausea and even abdominal pain.

Cushing suggesting that there may be a vomiting center, asserting that vomiting is more common in lesions involving the bulb. He also says that it is absent in two-thirds of the cases.

*Choked Disk.*—Choked disk is perhaps the most important of the general signs of brain tumor, because it is subject to less variation, and is almost always present. The choked disk, according to Oppenheim, is absent only in about 10 per cent. of brain tumor cases, being almost invariably present at some time or other in the other 90 per cent. In the very early stages the veins become distended and then tortuous. The papilla becomes somewhat injected and the margins, beginning usually with the nasal side, become less sharply defined. Then the arteries become less prominent on one side, usually the side on which the tumor is located. The disk then becomes swollen, projects into the vitreous humor, at times fountain-like. The arteries disappear and the veins may appear to fall back to the general level of the retina. In this stage there is no difference in color between the papilla and the retina. Small hemorrhages are seen about the margins of the swollen, edematous area. If the swelling still increases, the area of the papilla becomes more opaque and the hemorrhages increase in size. If no relief to the intracranial tension is given, the vascularity then diminishes, the disk becomes pale, and atrophy sets in; the swelling, however, may persist or diminish, but the vision gradually decreases and ends in blindness.

After decompression, the choked disk subsides gradually. If the intracranial tension is not completely relieved, the swelling may continue, but usually there is a marked decrease even with a good-sized

bulging of the scalp, as is seen especially after cerebellar decompression.

There is no fixed rule as to whether or not the partial atrophy of the optic nerve, which is present before either a radical or a decompressive operation, may be brought to a standstill. In some cases, the atrophy goes on until complete blindness supervenes; in others, the vision, after the operation, remains the same or is even improved. Surgical measures should, therefore, be undertaken before the acuity of vision begins to diminish. The occurrence of choked disk in one

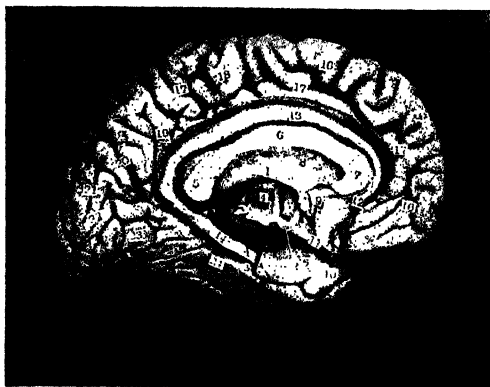


FIG. 13.—BRAIN AREAS (Campbell).

eye earlier than the other is no very certain sign for localizing the tumor in that hemisphere, nor is the size of the choked disk an indication of subtentorial growths, although the intracranial pressure is greater in the latter location than when the tumor is located elsewhere.

A syphilitic exudate into, and a swelling of the papilla from, the same cause must be borne in mind when diagnosing a choked disk; for the general and local symptoms of syphilitic basilar meningitis may closely resemble a brain tumor symptom-complex.

*Dyschromatopsia*.—Interlacing and inversion of the color fields have been demonstrated by Cushing to be not only a very constant sign of brain tumor, but he has found it on several occasions to be demonstrable before any swelling of the disk was present.<sup>19</sup>

Although all the color fields may be affected, the blue field is affected more markedly than the others, its boundaries interlacing with and at times becoming completely inverted within those of the red field.

*Hemichromatopsia*.—Hemichromatopsia is also described by Cushing, and he avers that the loss of color perception may precede the loss of perception for form, thus foretelling an impending hemianopsia and showing as a localizing as well as a general symptom. Cushing

is inclined to look upon dyschromatopsia as a sign of increased intracranial pressure, normal color field quickly returning after decompression.

**Convulsions.**—Convulsive seizures seen in brain tumors are of three types: general convulsions, focal epilepsy (jacksonian), and cerebellar spasms. The latter two forms will be considered under regional signs.

General epileptic seizures occur rather infrequently in brain tumors, but may occur at any period of development. They are of special interest when the attacks precede all of the general and focal signs. In one of the author's cases severe epileptic seizures, with unusual abdominal pain and prolonged unconsciousness and delirium, preceded the general and focal symptoms by three months. These epileptiform seizures cannot be distinguished in any way from so-called genuine idiopathic epilepsy.

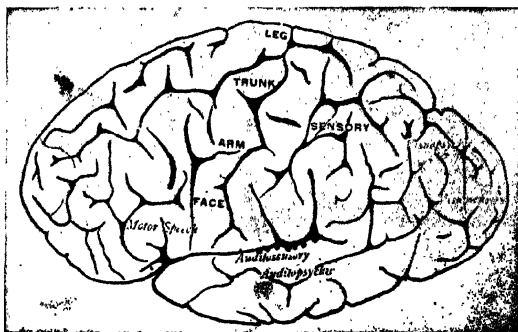


FIG. 14.—FUNCTIONAL AREAS OF THE CEREBRAL CORTEX OF THE LEFT SIDE.  
(After Campbell.)

**Intelligence and Consciousness.**—With the exception of frontal lobe tumors, the change in consciousness and intelligence is usually quantitative. Although brain tumors are found quite frequently in autopsies on the insane, they rarely cause insanity. The patients are usually somnolent and apathetic. This condition is subject to exacerbations and remissions, and is usually most marked during the attacks of severe headaches. When aroused, the patient can give an account of himself and is oriented for time and place. In severe cases this apathy may be mistaken for dementia. At least one patient was referred to the writer for parietic dementia who had a tumor of the left gyrus angularis.

**Pulse.**—The pulse rate is a general sign of brain tumor only when it is abnormally low. A violent headache, projectile vomiting and a slow pulse rate are usually seen simultaneously when intracranial pressure is greatly increased.

**LOCALIZING SIGNS.**—There are to-day known to be very few *silent areas* in the brain. A tumor, by pressure or infiltration, leads to a definite disturbance or a loss of function of some area of the cortex or

subcortical tissue, or of the brain-stem or cerebellum. It is by a careful analysis of the progress of this disturbance of function that a tumor can be localized. In a general way, in the cerebrum, a tumor is cortical or subcortical. If possible, we ought to be able to say from the chronological order of development of the symptoms whether the growth is of the one character or the other. We may say that growths which have their origin from the membranes or calvarium and compress the cortex will first manifest irritating signs and later on will produce loss of function. The loss of function will be somewhat limited, at least in the early stages of the growth. Thus a small tumor in the motor area of the cortex will at first cause a strictly jacksonian spasm, for instance in the facial group of muscles. The muscles themselves will

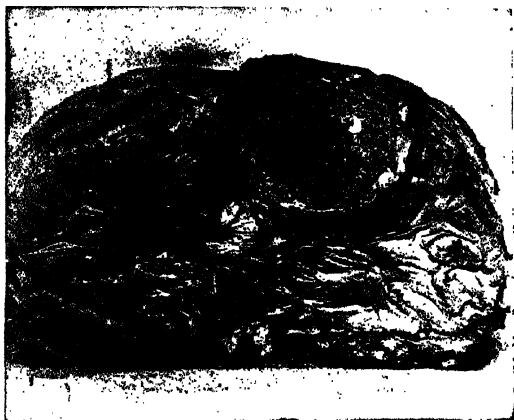


FIG. 15.—LARGE TUMOR OF THE RIGHT PARACENTRAL CONVOLUTION.

not be paralyzed at first. Only later will the facial group show loss of function by being weak. On the other hand, subcortical growths will cause a primary destruction of brain tissue with primary loss of function. Hence, in subcortical growths of the motor zone, paralysis will not be preceded by jacksonian seizures, and we are apt to have a monoplegia, or even a hemiplegia early in the stage of the tumor development.

Sometimes the tumors produce distal symptoms which may confuse. Thus a tumor (Fig. 15) which grew in the paracentral convolution of the right hemisphere, by pressure on the paracentral convolution of the other side caused spastic symptoms, ankle clonus and Babinski sign on both legs, which was constant on the left leg and present at one time and absent again in a few days on the other side. Another tumor, growing into the longitudinal fissure, came under our observation with total blindness, but its history pointed to a hemianopsia first and total blindness later. The operation revealed a growth pressing on, but

not destroying, both cunei, and its removal was followed by a recovery of sight. Cushing has pointed out how a paralysis of the sixth nerve, by being constricted by a branch of the basilar artery, can be a confusing distal symptom in a tumor located almost anywhere.

The repeated occurrence of internal hydrocephalus, as illustrated by case in Figures 9 and 10, may for a long time obscure the focal symptoms.

Tumors in silent areas may produce distal symptoms and cause us to make errors in localization. Thus, Oppenheim refers to a cerebellar tumor causing such a pressure upon the occipital lobe that localizing occipital signs were produced; and Cushing refers to a tumor of the occipital lobe compressing the cerebellum.



FIG. 16.—TUMOR OF THE PREFRONTAL AREA.

Focal symptoms, like the general symptoms, must show a steady progression in the extension and number of signs from a small beginning to the fully developed picture caused by a destruction of tissues and a consequent loss of function. By carefully studying the development of the signs in their chronological order we can usually locate the tumor and indicate with a fair degree of accuracy what are the real signs, and what are the neighborhood and distal signs.

*Tumors of the Frontal Lobe.*—We must distinguish between prefrontal tumors—mainly, tumors anterior to the ascending frontal convolution—and tumors primarily situated in the ascending frontal or the motor area. The latter will be considered under a special head.

We ought also distinguish between tumors of the convex surface of the white substance, and tumors which primarily affect the orbital surface. Perhaps we ought also distinguish between growths of the right and growths of the left frontal lobe, because the latter, in addi

tion to affecting the Broca center for motor speech, are also supposed to have a more marked effect with regard to the intellectual functions.

We may say with a fair degree of certainty that cortical and sub-cortical tumors of the prefrontal area, especially on the left side, have a definite syndrome (Fig. 16). The first and earliest manifestations are mental deterioration, defective judgment, lapses of memory, a staggering gait, and a tendency to fall to the opposite side (frontopontine cerebellar tract). Puerile joking and punning is sometimes observed (Witzelsucht). Knapp insists that nearly all forms of mental disease can complicate brain tumors. Blackburn found 29 tumors in 1,642 autopsies among the insane. Most of these cases showed profound dementia. In only three cases was the diagnosis made during life. In the others no clear previous history was present, and the dementing process had advanced so far as to obscure all signs of brain tumor during life.

Later on, by compressing and irritating the adjoining tissues, we have motor speech disturbances and jacksonian epileptic seizures, and last of all monoplegia and hemiplegias of a spastic character.

Starr states that tumors of the orbital surface do not cause mental symptoms. That there are at least exceptions to this statement is proven by the tumor in Figure 8. This tumor, about the size of a tangerine, grew from the hypophysis and caused progressive atrophy of the optic nerve, and growing, as it did, almost symmetrically against the lower surface of both frontal lobes, it caused progressive dementia. The loss of pupillary reflexes, the atrophy of the optic nerve without choked disk, and the progressive dementia caused the case to be diagnosed as parietic dementia. There were never any signs of intracranial pressure. The tumor was found on autopsy.

Lately, J. Foster Kennedy<sup>20</sup> has called attention to the following syndrome, previously sketched by Oppenheim,<sup>21</sup> produced by expanding lesions of the orbital surfaces of the frontal lobe: (1) signs of true retro-bulbar neuritis, central scotoma, progressive loss of acuity of vision and a primary atrophy of the optic disk on the side of the lesion; (2) ipsilateral anosmia; (3) papillo-edema of the opposite side.

The explanation of the syndrome is as follows:

The growth primarily compresses the optic nerve on the side of tumor, and, by thus mechanically obliterating the sheath surrounding the optic nerve, prevents the increased intracranial pressure from producing a papillo-edema on that side, whereas the latter condition is free to develop on the opposite side.

The central scotoma is the result of the fact that the bundles going from the macula are in the central part of the optic nerve and are more delicate in structure, therefore succumbing more easily to pressure. Later on the entire optic nerve is destroyed, with gradual loss of acuity of vision and a primary atrophy of the optic nerve as the results. The anosmia is caused by a destruction of the olfactory bulb.

In the view of the above case (Fig. 8) we not only confirm Kennedy's contention of a primary atrophy of the optic nerve without a preceding

papillo-edema, but might add that if the tumor is large enough, progressive dementia would be the terminal stage of this syndrome, more especially perhaps in tumors on the left side.

*Tumors in the Psychomotor Area.*—The psychomotor area is situated in the prerolandic area, and in the paracentral convolution. It occupies the ascending frontal convolution on the convex surface, and perhaps the entire paracentral convolution on the median surface of the brain. Growths starting from the membranes and compressing the cortex have, as their first manifestation irritative signs, usually localized spasms of groups of muscles on the opposite side of the body. These spasms are known as jacksonian epileptic seizures. In the beginning they may affect only small groups of muscles, like the facial and perhaps the lingual, or they may be limited to the flexors of the forearm. At times they remain localized to the original group, and they invariably begin in the same group of muscles. Later on, however, the convulsive seizure spreads to the remaining muscles on the same side of the body, and then to the opposite side. There are two characteristics of these seizures: the first is that the convulsion always begins in the same group; the second, that the patient preserves consciousness as long as the attack remains confined to one side of the body. Unconsciousness sets in only when the attack becomes general. If the loss of consciousness precedes the localized convulsion it is not a jacksonian convulsion, and has no special diagnostic significance. Every jacksonian seizure is not a sign of brain tumor; it is always, however, an indication of a focal irritation of the motor area. Cushing<sup>22</sup> has reported two cases of persistent spasm of the facial group of muscles, one of which was mistaken for a cortical spasm, as being caused by tumors of the cerebellopontine angle. These exceptional cases differed from the ordinary jacksonian facial spasms in that they persisted for years, without extending to the arm and leg of the same side. These exceptions, however, by their extreme rarity only confirm the foregoing rule. In these cases the involvement of the acoustic and the presence of bulbar compression symptoms would enable us to rule out a tumor of cortical origin. Every jacksonian epileptic seizure, however, should arouse our suspicions, and put us on our guard. Even though all general signs of brain tumor may be absent, the jacksonian seizure may be the earliest manifestation of a growth, and only when the latter has attained a sufficient size are the general symptoms developed. This may require months or even a year or more, and we should therefore be very conservative in giving a definite opinion.

Soon, however, the jacksonian epileptic attack is followed by a paresis of the group of muscles in which the attack originated. This paresis is at first only of short duration and completely disappears; but as time goes on it becomes of longer duration and increasingly pronounced, until finally it is present in the interval between the jacksonian attacks. The character of the paralysis is that of an upper motor neuron type spastic, with increased deep reflexes and, in the lower extremities, with ankle clonus and Babinski sign. The type of the cortical paralysis "

the monoplegic type, although we may have the arm, face, or the arm-leg combination.

Tumors of the paracentral convolution on the median surface, by causing pressure symptoms of the opposite paracentral convolution, may occasionally cause some confusion as to exact localization. Thus a case of brain tumor, with jacksonian seizures and right-sided hemiplegia at intervals, presented a spastic paresis of the left leg with ankle clonus and Babinski sign (Fig. 15).

Sensory disturbances are seen at times in both irritative and destructive lesions of the motor zone. In one case\* of jacksonian seizure, caused by a tumor of the arm center, the convulsion was preceded by a sharp pain in the index finger. In another case,\*\* in which the tubercle was successfully removed, the paretic hand showed a typical astereognosis.

Although we must hold with Mills, that the stereognostic sense is the special function of the superior parietal convolution, nevertheless, there are exceptions to the rule, as is proven by cases of cortical extirpation of the motor zone followed by astereognosis (Hoppe<sup>24</sup>).

In other cases, loss of the stereognostic sense followed the removal of a tumor of the motor area (Taylor, Dana, Paggio, Hoppe; see Hoppe for literature) and was not present before the operation.

It is possible, but not proven, that astereognosis, unassociated with loss of tactile and muscle sense, would indicate a lesion of the motor zone; and astereognosis, with loss of tactile sense, muscle sense, and sense of position, would indicate a lesion of the parietal zone. Both Kraus and Rasumosky have reported cases in which excision of the motor cortex was followed by loss of sensation in all its qualities. Patrick reports a well observed case of a small lesion of the ascending frontal convolution causing sensory disturbances in various qualities.

We have the rather paradoxical situation that pathological lesions of the motor zone rarely produce loss of sensation; whereas, excision of the cortex is followed by such a disturbance. We simply have to fall back on the old theory that sensory impressions can be perceived by various areas of the cortex, that sudden removal of the centers by excision is followed by loss of sensation, which in most instances clears up, but occasionally persists for a long time; but, on the other hand, that slowly developing pathological lesions, such as brain tumors of the motor zone, although they produce subjective disturbances of sensation, except in rare instances, show no objective sensory signs. We must, therefore, clinically and for the purpose of localization, adhere to a strict separation of the motor and sensory areas of the cortex, the rolandic fissure being the dividing line.

*Tumors of the Parietal Lobe.*—For the purpose of localization we must divide the parietal lobe into three sections: the ascending parietal convolution; the superior parietal convolution; and the inferior convo-

\* A clinical and pathological contribution to the study of the central localization of the sensory tract. Hoppe.<sup>25</sup>

\*\* A critical study of the sensory functions of the motor zone (pre-rolandic area) more especially stereognosis.<sup>26</sup>



lution, which contains the gyrus angularis and the gyrus marginalis.

The ascending parietal convolution is a sensory area, and perhaps contains centers for tactile, muscle and temperature sense, as well as pain sense, for regions of the body whose adjacent centers in the ascending frontal lobe preside over the motor functions. Tumors of this area may have as their initial manifestation subjective sensory symptoms; we may call them sensory jacksonian seizures. But very often as the tumor increases in size, by irritation, compression and destruction of the adjacent prerolandic areas, they cause jacksonian convulsions and monoplegia. The convulsive and paralytic manifestations are distal pressure symptoms. Oppenheim claims that we often have a dissociation of sensory manifestations, and that the latter is always a partial



FIG. 17.—TUMOR OF THE SUPERIOR PARIETAL CONVOLUTION.

hemianesthesia; for pain and temperature senses are preserved, while tactile sense and sense of position are impaired and lost.

If the superior parietal lobe is the seat of the growth, the most characteristic sign is the loss of the stereognostic sense. The patient is unable, with closed eyes, to recognize the shape, surface conditions and weight of an object placed in the hand of the opposite side. This function of the superior parietal convolution was first described by Oppenheim.

Starr and McCosh, and later Spiller, described cases showing that lesions of the superior parietal convolution cause a loss of the sense of position and ataxia of the limbs of the opposite side of the body.

Very characteristic, therefore, of tumors, both cortical and subcortical of the superior parietal convolution (Fig. 17), are astereognosis, loss of the sense of position and ataxia of the opposite extremities, with

impairment of tactile sensation, and in a less degree of pain and temperature sensations.

Spiller, Potts and Dercum have placed on record tumors of the pons and medulla with loss of the stereognostic sense (Posey and Spiller<sup>25</sup>).

The above sensory losses must be associated with motor disturbances of such a character as to enable us to localize the lesion in the cerebrum rather than subtentorially. Occasionally a tumor can be observed so early as to enable us to locate it in the gyrus angularis, more especially if it is on the left side. Thus, a recent case first showed some alexia, then hemianopsia, and sensory aphasia (mind-blindness), which enabled us to locate the tumor immediately in and below the gyrus angularis of the left parietal lobe.

A subcortical tumor of the parietal lobe, rather large in size, may cause, by pressing upon the internal capsule, hemiplegia, hemianesthesia and hemianopsia, the combination being very distinctive of the parietal lobe (Spiller).

*Tumors in the Occipital Lobe.*—Memory pictures for vision are associated with the convex surface of the occipital lobes, but destruction of one side does not produce mind-blindness. It is only when the convex surface of both lobes is destroyed that the memory pictures are lost. Tumors of the convex surface therefore are apt to produce no localizing manifestations. There are, however, cases on record (Oppenheim and Spiller) which seemed to show localizing signs. These signs are visual hallucinations observed in the opposite visual field. These visual hallucinations may be pictures, but are more often spots, lines and flashes of light. They have been observed to occur in the form of attacks of sensory jacksonian epilepsy (visual) (Bramwell). They may precede the development of a homogeneous hemianopsia, and they may occur periodically in the blind field.

We must, however, be on our guard, for visual hallucinations and illusions may occur in intra-ocular disease (Oppenheim-Uthoff). Spiller speaks of a case of retinal hemorrhage in which the patient, among other hallucinations, saw horses. We must also remember (Jolly-Pick) that irritation of the optic tract fibers causes scintillating scotoma.

Tumors of the median surface of the cuneus produce homonymous hemianopsia with normal pupillary light reaction. This hemianopsia may be preceded by hemiachromatopsia. In these cases we may have total blindness, with recovery, as occurred in one of the author's cases, if the tumor is so located as to produce pressure on the opposite cuneus. We can also have total blindness, due to atrophy of the optic nerves after papillo-edema; and thus, of course, recovery of sight will not follow a successful operation. In these cases, as in those of the authors cited above, the history of a hemianopsia preceding total blindness will enable us to localize the tumor. Cushing calls attention to the fact that large tumors of the occipital lobe by pressure on the cerebellum may cause cerebellar symptoms. Oppenheim has recorded just the opposite: viz., tumor of the cerebellum which caused occipital symptoms.

On the left side a subcortical occipital tumor, located somewhat anteriorly so as to intercept the association fibers from the gyrus angularis and those to the temporal lobe, may cause alexia, word-blindness and hemianopsia (Fig. 9).

The syndrome rather characteristic, therefore, of occipital lobe tumors is: a progressive hemiachromatopsia, preceding a homonymous hemianopsia, with perhaps visual hallucinations, and then blindness with intact pupillary light reaction.

*Tumors of the Temporal Lobes.*—The right temporal lobe in right-handed people is undoubtedly a silent area, because ordinary auditory memory pictures seem to have a bilateral representation, and destruction of one temporal lobe does not produce deafness in the opposite ear. For this very reason, a tumor which cannot be located in any other part of the brain is apt to be located in the right temporal lobe. Cushing uncovered four tumors in this region in the ordinary decompression operation.

On the left side the characteristic focal sign is amnesic aphasia; this is especially true of subcortical growths. If the growth is very large we may have a mixed aphasia of the amnesic type. In other growths extending backward and upward, the amnesic aphasia may be associated with alexia and hemianopsia, due to an involvement of the association fibers between the first temporal convolution and the occipital lobe.

Tumors of the tip of the temporal lobe below the gyrus uncinatus may lead to uncinate fits. Thus one of the author's patients had epileptic seizures, in which the primary manifestation was a subjective sense of a nasty odor or smell, coming from the throat, attended with profuse salivation and attempts at swallowing. In quite a number of cases this symptom has been of localizing value.

*Tumors of the Corpus Callosum.*—These tumors are rarely limited to the corpus callosum, but grow into the gyrus fornicatus and the white substance of both hemispheres.

The corpus callosum is the great association tract which brings the two hemispheres into harmonious relation, and brings identical areas of the cortex of the two hemispheres into function.

Bristow's syndrome is the one accepted: viz., marked deterioration of the mental faculties, hebetude, apathy, and placid coma, hemiparesis of both sides of the body, somewhat less on one side, and an absence or only a minor degree of the general signs of intracranial pressure. Oppenheim calls attention to the fact that the above symptoms are rather negative in character. Bruns warns us that we can localize growths in the corpus callosum only with great reservation.

On the other hand, tumors of the corpus callosum may occur without producing any destructive symptoms whatever.

*Tumors of the Basal Ganglia.*—Tumors of the nucleus lenticularis and of the nucleus caudatus produce no specific syndrome except through pressure on the internal capsule. In one case the very marked spastic hemiplegia was preceded by spasms in the arm, which were more or less continuous and, while simulating jacksonian seizures, were of longer

duration and the rigid condition of the muscles did not relax in the interval between attacks. The closer the tumor is to the cortex in the centrum semiovale, the less extensive the paralysis; the deeper the tumor, the more the paralysis approaches a complete spastic hemiplegia.

These tumors necessarily, by breaking down the association tracts, cause marked mental and often mixed speech disturbances. Thus a case (Figs. 2, 3, 4) showed mental disturbance, great apathy, amnesic aphasia, astereognosis, and the patient had a single attack of jacksonian epilepsy. Complete hemiplegia developed later on.

*Tumors of the Thalamus Opticus.*—Tumors of the thalamus give rise to a more marked syndrome which lead often to an approximate localization. In one case (Figs. 9-10) the entire optic thalamus was destroyed by a tumor of the size of a hen's egg. For four years this patient had intermittent attacks of internal hydrocephalus. A rather typical syndrome was developed during the last fourteen months of his life. The first manifestation was a left-sided hemianopsia, with pupils reacting normally to light, then a paresis of the left side of face. This was followed by a weakness of both legs, bilateral Babinski, bilateral ankle clonus with a staggering gait. (The spastic bilateral phenomena occurred during an attack of hydrocephalus, disappearing when the latter condition subsided.) Later on there developed blindness due to atrophy of the optic nerves, left-sided Babinski, but no ankle clonus, right patellar reflex being absent. At this period patient laughed immoderately without adequate cause. This case at no time showed any sensory disturbances. The only fixed continuous sign was the hemianopsia, the contralateral paresis, and the ataxia of both upper and lower extremities with very marked Romberg sign. At no time was there any pain in the left extremities. The patient also showed the forced laughter and the staggering backward which Beever describes.

Spiller<sup>26</sup> has given a most careful analysis of the cases of thalamic tumors. The one constant symptom is hemianopsia. This, however, is denied by Bramwell, but generally accepted by all other observers. Then there is usually some spastic weakness of the extremities of the opposite side, often with either ataxia or choreic or athetoid movements. Sensory disturbances are not so constant. Some of the cases are characterized by attacks of pain in the opposite extremities.

Total blindness is always secondary to papillo-edema. Outbursts of laughing and crying are seen in some cases. The author's case, like Brewer's, showed a tendency to fall backward and to the side of the lesion. Bilateral symptoms, as in the case cited above, are due either to a complicating internal hydrocephalus, or to the projection of the tumor into the ventricle and to pressure on the opposite thalamus.

*Tumor of the Third and Lateral Ventricles.*—The tumors of the third ventricle were collected and reviewed by Weisenberg.<sup>27</sup> He was able to collect 30 cases up to 1910. He divides these tumors into three groups:

- (1) Those which are rather small, do not reach to, and do not occlude the foramen of Monro.

(2) Those which do reach and occlude the foramen of Monro.

(3) Those which extend into the aqueduct of Sylvius, infiltrate and destroy the surrounding tissue, and extend as far as the cerebral peduncles and the pons.

Internal hydrocephalus was present in all cases except three.

In the first group we have only symptoms of internal hydrocephalus: viz., headache, choked disk, nausea, vomiting and vertigo. If the tumor is large, pressure may be exerted on the internal capsules, producing spastic paresis of the extremities.

The second group presents practically the same symptoms as the first.

In the third group we have symptoms which very closely approximate the syndrome of corpora quadrigemina tumors, described farther on. These symptoms result from a destruction or compression of the nuclei of the third nerve, the nucleus ruber, the superior cerebellar peduncle and the posterior longitudinal bundle. The chief symptoms are disturbance of the associated ocular movements, cerebellar ataxia, ptosis of one or both lids, pupils widely dilated, with sluggish light reaction, unilateral or bilateral exophthalmus. There is weakness of the extremities. The tendon reflexes may be exaggerated, diminished or normal. The general symptoms of brain tumor are always present.

These tumors originate from the ependyma or from the choroid plexus.

*Tumors of the Hypophysis* (Fig. 8).—Tumors of the hypophysis produce twofold symptoms:

(1) Those caused by an interference, either by pressure or by destruction, of the specific function of the hypophysis.

(2) "Neighborhood symptoms" caused by the pressure of the tumor on the structures in the intrapeduncular space and the orbital surfaces of the frontal lobes.

*I. Symptoms Caused by an Interference.*—In order to consider properly the symptoms caused by an interference with the functions of the hypophysis, let us consider a brief résumé of our present knowledge of the hypophysis.

The physiology of the hypophysis after twenty-five years of work, investigation, and a perfect avalanche of literature, is still unsettled. We know that it is a ductless gland which stands in intimate relation with the thyroid, the parathyroids, the thymus, suprarenals, the islands of Langerhans and the sexual glands. Like all ductless glands, it secretes, according to Schaefer,<sup>28</sup> "hormones," activating and stimulating substances, with obscure but important effects on numerous organs, ductless, sexual and others, as well as upon metabolism in the broadest sense, including growth.

It is also certain, from the experiments, that the anterior and posterior lobes have entirely different functions. Paulesco was able to show, in 1908, and his observations have been verified by Cushing,<sup>29</sup> Homans, Crowe and others that the pituitary body is essential to the maintenance of life; that the total removal leads, in the course of

days or weeks, to death from a cachexia hypophyseopriva which resembles in many ways the cachexia strumipriva. Cushing<sup>30</sup> states that partial removal of the gland leads to a peculiar adiposity, polyuria, glycosuria, shedding of hair, and occasionally unmistakable lessening of sexual activities, even with atrophy of the testicle and ovaries.

Nobody has been able to produce a condition simulating acromegaly in an experimental way. Clinically and pathologically we have some facts relating to the absence or excessive function of the hypophysis.

Congenital absence of the hypophysis has been observed in cretins. Virchow found an almost entire absence of the anterior lobe in a newborn cretin.

Benda<sup>31</sup> found a small defective hypophysis in a 38-year-old dwarf. Frölich's<sup>32</sup> case was a dwarf. On the other hand, the hypophysis is usually found greatly enlarged in giants. This has led to the theory that overactivity of the hypophysis in early life leads to gigantism, and, later, after development has been completed, to localized overgrowth, manifesting itself as acromegaly.

The question of growth and its relations to the functions of the hypophysis has received an interesting contribution when it was found by Erdheim and Stumme<sup>33</sup> that the hypophysis is always enlarged in pregnancy, often to two or three times its normal size. This increase is found to be due to a true hyperplasia of the secreting cells of the anterior lobe. According to Kohn,<sup>34</sup> this increase of the hypophysis during pregnancy and lactation can be compared to what occurs in gigantism. The pregnant woman is in a temporary state of overgrowth—not only does her own body increase in weight, but she grows an entirely new body within herself—and this demand for development is associated with a true hypertrophy and increase in function of the hypophysis. Early castration, before the completion of development, in both animals and men (eunuchs) is associated with an enlargement of the hypophysis, as well as overgrowth. Castrated animals grow larger than non-castrated, and so also eunuchs attain, very often, a large size. At the same time there is a change in secondary sexual characteristics, well known and needing no special mention.

When maturity has been attained, as Benda and Kohn have shown, castration is followed by an enlargement of the hypophysis, but not beyond the maximum normal size. There is no doubt an interrelation of the hypophysis and the testes, ovaries and the sexual function. Moyer<sup>35</sup> says that the impulse starts from the testes and ovaries and not *vice versa*. He looks, for instance, upon acromegalic changes as having their origin in the sexual glands, and the hypophysis as being affected only secondarily.

Is sexual non-development or sexual infantilism in the adult a manifestation of hypopituitarism? In an experimental way we have the researches of Cushing, who states that partial removal of the gland leads to a peculiar adiposity, shedding of hair, unmistakable lessening of the sexual activities and even to non-development of the testicles and ovaries. Frölich's description of dystrophia adiposogenitalis, viz., small stature,

infantile genitalia, hypotrichosis and an excessive deposit of fat, are looked upon as manifestations of hypopituitarism. Cushing, perhaps, having in mind cases like the one described above, says that we may have an overlapping of symptoms: viz., acromegaly with sexual infantilism, occasioned by a hypersecretion of one part of the gland and a diminished secretion of another.

This leads us to an opinion lately expressed by B. Fisher Frank<sup>36</sup> that acromegaly is the result of a specific hypersecretion of the anterior lobe of the hypophysis, and that dystrophia adiposogenitalis is due to a damaged condition of the posterior lobe and the infundibulum. On the other hand, Kohn holds that hypogenitalism is associated with an enlargement of the hypophysis.

The fact that tumors of the hypophysis, as in the cases of Schloffers and Hochenegg, caused infantile characteristics in the first, and heterosexual characteristics in the second, does not prove that there was an increased activity of the hypophysis. The removal of the tumors in the above cases was followed by sexual changes toward the normal. There may just as well have been a diminution of the glandular activity as a result of pressure, with a return of normal gland activity as a result of the removal of pressure. Kohn concludes, however, that as a result of excessive function of the hypophysis, the development of secondary sexual characteristics is inhibited. We are apt to associate excessive function of an organ with an increase in size; although this is not necessarily true, if we accept the researches of Benda and Lewis,<sup>37</sup> mentioned above. Acknowledging the relation between the hypophysis and the sexual system, it is of the greatest therapeutic importance to determine whether hypogenitalism causes hypoplasia of the hypophysis, or whether, as Kohn would have us believe, hyperfunction of the hypophysis leads to hypogenitalism.

Is the relation between these various organs of internal secretion vicarious in its nature? Does the overaction of one supplement the want of activity of the other, supplying a certain lack in function, or is there a rivalry, an antagonism, between them? Does the excessive activity of the one inhibit and cause a minus activity of the other? This interaction or interference of these various organs will lead to pluriglandular symptoms, but we must not conclude that there is of necessity pluriglandular disease. Primarily one may be diseased, and the function of several others thereby disturbed. A plus action of the hypophysis may cause acromegaly, and we may at the same time expect a hypogenitalism and a hypothyroidism (Kohn). There being an undoubted relation between the genital organs and the thymus and suprarenal capsules, we might, starting with hyperactivity of the pituitary gland, in addition to the above condition, find a persistent thymus and enlarged suprarenals. This system of correlation is complex, and the symptoms will be numerous, if the dictum is true that a disease of one gland of internal secretion will interfere with the functions of the others.

As generally understood to-day, hypersecretion of the hypophysis leads to excessive growth, and in young individuals leads to gigantism,

either pure and simple, or giantism with more or less acromegaly with general and sexual weakness. If it occurs after the completion of development, it manifests itself in localized overgrowth which clinically presents itself in the form of acromegaly.

Hyposecretion of the anterior lobe manifests itself in a lowered state of nutrition and growth, in dwarfism, in sexual infantilism and perhaps in the development of heterosexual characteristics. Cushing<sup>38</sup> has shown that the posterior lobe is essential to effective carbohydrate metabolism, and that a diminution of the posterior lobe secretion leads to an acquired high tolerance for sugars, with resulting accumulation of fat.

As Cushing says, this is a convenient working hypothesis. It is probably not as simple as all this, and on account of the interrelation of the hypophysis and the disturbances produced by a diseased condition, will be difficult to determine and to separate from those due to a disordered function of the other ductless glands, caused by the disease of the hypophysis.

Because of the obscurity involving this subject the writer believes it appropriate to give the conclusions which A. Munzer<sup>39</sup> draws from a very exhaustive review of the anatomy, physiology, and pathology of the pituitary body. Concerning the physiology, he says:

(1) It is not positively proven, but probable, that the hypophysis is necessary to life.

(2) The functional mechanism of the hypophysis has not as yet been satisfactorily explained; the colloid is probably the most active secretion of the gland.

(3) The toxicity of the hypophysis is small and probably depends exclusively on the posterior lobe of the gland.

(4) Hypophysectomy causes a cachexia hypophysipriva which is very similar to cachexia strumipriva.

(5) The hypophysis influences the circulatory apparatus through the posterior lobe.

(6) The hypophysis takes a part in regulating tissue metabolism.

(7) The hypophysis extract acts upon involuntary muscles and dilates the pupils.

(8) The hypophysis stands in correlation with other organs of internal secretion.

(9) The physiology of the hypophysis gives us no reason or explanation for the development of acromegaly.

His conclusions from the study of the pathology are as follows:

(1) The pathologico-anatomical processes of the hypophysis are (a) atrophic conditions; (b) hypertrophic-hypoplastic conditions; (c) tumors.

(2) We must distinguish between the clinical symptoms of hypophysis tumor, differentiating those which are caused by mechanical pressure, and those due to a disturbance of the function of the gland.



(3) The eye symptoms are the chief mechanical pressure symptoms.

(4) Acromegaly is probably not the expression of a primary change in the hypophysis.

(5) The reason of the occurrence of dystrophia adiposogenitalis with hypophysis tumors has not been cleared up.

That acromegaly has an undoubted relation to disturbances of the hypophysis the many cases on record of tumor and disease of the hypophysis clearly show. This theory is so universally accepted that we always expect a tumor of the hypophysis when we diagnose the condition clinically. But the fact that hypophysis tumors often occur without causing acromegaly seems to indicate that whatever disturbance is caused in the functions of the hypophysis may be vicariously neutralized by some of the other ductless glands. Moreover, there are cases to indicate that either excessive actions of the hypophysis can exist without a marked increase in structure, or that the normal action of the gland can be inhibited by the action of some other ductless glands, the clinical picture produced being one of hyposecretion. One fact, however, stands out prominently in this discussion: there are few cases of acromegaly on record in which some changes were not found in the hypophysis. On the other hand, changes in the other ductless glands are not at all constant, and hence the line of investigation will continue in the direction of pathological changes in the hypophysis.

Cushing, on account of the failure clinically to classify cases as due either to hypo- or hyperfunction of the glands, suggests that it is more suitable to employ the term dyspituitarism. On a basis of 50 clinical cases occurring in his own practice, he divides the cases in five groups:

(1) Cases which show both neighborhood symptoms as well as disturbed function of the gland.

(2) Cases in which the neighborhood symptoms are very pronounced, and disturbed function of the gland are absent or inconspicuous.

(3) Cases in which the neighborhood symptoms are absent and the glandular symptoms are marked.

(4) Cases in which the glandular symptoms are secondary to distant cerebral lesions.

(5) Cases of polyglandular disease in which the hypophysis changes are only a part of, and not the predominant manifestation of, the disease.

We must bear in mind, however, that we may have tumors of the hypophysis without any manifestations of perverted secretion; also that typical cases of acromegaly or of Frölich's disease are encountered with no macroscopic changes whatsoever in the size of the hypophysis.

Under each of the first four groups there will naturally occur three subdivisions, namely:

(1) The cases in which hyperpituitarism, more particularly overgrowth, predominates: (a) resulting in gigantism, when the process antedates ossification, Typhus Launois; (b) resulting in acromegaly, when it occurs later.

(2) Those in which the clinical symptoms of hypopituitarism predominate: adiposity with a persistence of both skeletal and sexual infantilism, when the process originates in childhood; adiposity with sexual infantilism of the reversible form, when it originates in the adult.

(3) The mixed or transition cases, exhibiting some features of both states; in other words, with evident dyspituitarism.

II. *Neighborhood Symptoms.*—Neighborhood symptoms are due chiefly to the pressure of the tumor on the optic tract and optic nerves. The first sign is usually a bitemporal hemianopsia, due to the fact that the pressure is first exerted on the optic chiasm. The pressure, however, may be unequal: one optic nerve may be compressed with the chiasm, leading to blindness of one eye; and there may be but a loss of the temporal field in the other. There is usually no choked disk in the beginning, because there is not much increase of intracranial pressure; but the optic disks undergo primary atrophy, and later on, when the intracranial pressure is increased, papillo-edema may develop in the atrophied nerve-head. The x-ray will show an enlargement of the sella, perhaps an absorption of the clinoid processes. Headache is usually marked, and an early symptom.

In analyzing 148 cases of hypophyseal disease, 101 of which were due to tumors, Cushing<sup>40</sup> states that among the 101 cases, 53 involved the gland and 48 arose from suprasellar sources. He divides the cases into two groups: those of intrasellar origin and those of suprasellar origin. Among the cases which showed neighborhood complications, the rule was that those manifesting glandular diseases were intrasellar, whereas those with adiposogenital dystrophy were of suprasellar derivation. There are, however, exceptions to this rule.

Moreover, the x-ray findings proved to be of great diagnostic value. They were of three kinds:

(1) The undeveloped sella. The sella is small and the symptoms are those of hypopituitarism without neighborhood symptoms, and hence, no tumor.

(2) The sella is distorted, irregular in outline, in a more or less abnormal position but normal in size. This condition of the sella points to a suprasellar tumor, or pressure.

(3) The sella, distended by a primary gland or struma.

We can see at a glance how important Cushing's study of the roentgenograms of his cases is from a diagnostic standpoint, and how much light it throws upon the question of surgical intervention.

The relation between diabetes insipidus and dyspituitarism has been made more than probable by the recent studies of Frank,<sup>41</sup> Simmonds<sup>42</sup>

and Cushing.<sup>43</sup> Some tumors of the hypophysis produce no glandular symptoms whatsoever. So also the general symptoms of intracranial pressure are absent, and the cases during life are mistaken for tabes or taboparetic cases. Figure 5 was a typical case of this character and one of the first to be published. Since then other cases have been placed on record by Oppenheim<sup>44</sup> and Kahlmeter.<sup>45</sup> In these cases there is a primary atrophy of the optic nerve, loss of patellar reflexes and progressive simple dementia. The *x*-ray will show changes in the sella which will clear up the diagnosis, if suspicions of sellar disease should be aroused.

That the function of the hypophysis and especially the posterior lobes may be interfered with, in internal hydrocephalus, by pressure from above, must be taken into consideration in the diagnosis of dyspituitarism. Cushing called our attention very early to this condition. Lately, Lewis J. Pollock<sup>46</sup> calls particular attention to the combination of chronic internal hydrocephalus and dystrophia adiposogenitalis.

We see, therefore, that any brain tumor or other lesion, no matter where located, may, especially in young individuals, by causing an internal hydrocephalus, be complicated by dyspituitarism, if the tumors are of slow development and cause chronic hydrocephalus.

*Tumors of the Pineal Gland.*—K. H. Krabbe<sup>47</sup> has published a monograph of 112 pages, in which he discusses all the facts and theories concerning the function of the pineal gland. The embryology, histology, and physiology are carefully considered. He states that in 70 cases only 5 showed the premature sexual development, and only a few showed obesity. He concludes that the function of the pineal gland is that of regulating and keeping constant the pressure of the cerebrospinal fluid. G. Horax<sup>48</sup> performed experimental pinealectomy on guinea pigs and noted that it hastened the sexual maturity of the animals. On the basis of these experiments, as well as on a study of 3 clinical cases, one with autopsy, he concluded that tumors of the pineal gland in children give rise to a syndrome characterized by precocious adolescence.

The characteristic syndrome in young individuals before the age of puberty, and especially in very young children, is precocious sexual development which is supposed to be caused by an altered internal secretion of the gland. In adults this complex is not seen, the only signs which are characteristic being neighboring symptoms, more especially pressure upon the region of the corpora quadrigemina, and therefore the signs and symptoms will approximate those of the latter region. Pearce Bailey and Smith Ely Jelliffe<sup>49</sup> describe a typical case and review the literature of 59 cases. They call attention to the fact that on account of the location of the gland the tumor presses upon the veins of Galen which drains the choroid plexuses and also presses upon the aqueduct of Sylvius; this causes an early and acute internal hydrocephalus which accentuates the general symptoms of increased intracranial pressure. These are early symptoms in pineal gland tumor. The metabolic symptoms are: (a) adiposis; (b) early sexual maturity; (c) cachexia. The adiposis is probably secondary, due to a disturbed func-

tion of the posterior lobe of the hypophysis, caused by the pressure of the internal hydrocephalus, and the picture may be that of the Frölich syndrome, *dystrophia adiposogenitalis*. The authors suggest that the precocious sexual development may be due to the character of the tumor, being more apt to occur in adenoma or teratoma, in which hyperfunction may be presumed to exist.

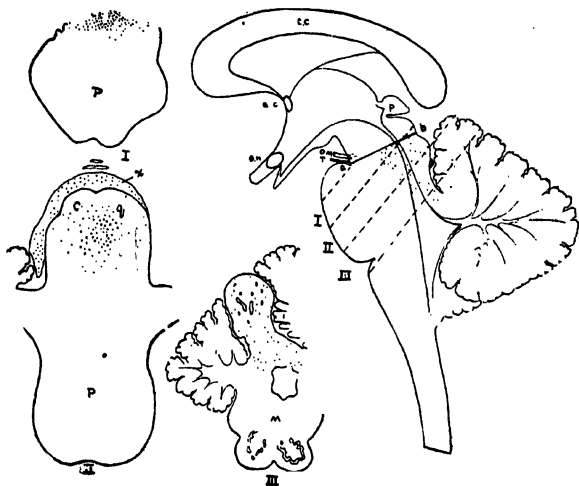


FIG. 18.—DIAGRAMMATIC SKETCH, SHOWING SAGITTAL SECTIONS THROUGH THE NORMAL BRAIN STEM.

*c.c.*, Corpus callosum; *p.*, pineal gland; *o.n.*, optic nerve; *o.m.* and *t.*, the oculomotor and trochlear nerves; *a-b*, the line of original section; I, II, III, the slices removed for sectioning; the dotted area, the approximate extent of the tumor.

Section I, from the anterior slice shows the pons, *p*; the dotted area, the extent of tumor involvement.

Section II, from the middle slice; *p*, pons; dotted area represents the tumor; *c.q.*, the site of the corpora quadrigemina; *x*, the tumor growth beyond the boundaries.

Section III, from the posterior slice; dotted area represents the tumor, *m*.

*Tumors of the Corpora Quadrigemina* (Fig. 18).—Tumors in this region are rather rare, especially those more or less limited to the region of the corpora quadrigemina. In the case illustrated, the symptoms were: double vision, staggering gait, falling to the right, gradual loss of vision, with total blindness after three or four months, sudden attacks of rigidity of all the muscles and falling to the ground, without loss of consciousness, atrophy of the optic nerves, loss of light reflex in the pupils, almost complete third nerve palsy in both eyes, normal hearing, ataxia with retropulsion, which became so extreme as to prevent the patient from standing or walking, with muscular power, sensation, and deep tendon reflexes normal.

After a rather complete study of the above case and the literature, we have concluded as follows: that neither blindness, deafness, nor ataxia is pathognomonic of a disturbed function of the corpora quadrigemina.<sup>50</sup>

(a) *Blindness*.—Ludwig Bach,<sup>51</sup> who worked up the literature up to 1899, concludes, from a critical study of all cases, that isolated destruction of the corpora quadrigemina in man does not cause blindness. Whether or not any disturbance of vision occurs at all, he says, cannot be determined definitely, although the answer seems to be in the negative (except through papillo-edema).

W. Nissen,<sup>52</sup> analyzing eight cases of tubercles in this region, concludes that destruction of the corpora quadrigemina does not produce blindness, no gross disturbance of vision having been noted in any of these cases.

It is true that our patient was blind, and that blindness set in with unusual rapidity; but we know that papillo-edema of an unusual degree occurred before the deterioration of vision, and that later on atrophy of the optic nerves was present. We can conclude, therefore, that blindness was caused by a degeneration of the optic nerves and not by a destruction of the corpora quadrigemina. This is probably true in many other cases. Moreover, it is our opinion that the tumor began in the corpora quadrigemina and must have destroyed, at least to a great extent, these structures, before it attained a size large enough to produce such a degree of intracranial pressure as to cause a very violent papillo-edema; and that, therefore, disturbance of vision, if caused by a destruction of the corpora quadrigemina, should have preceded the development of the papillo-edema, whereas we know that vision was normal, when the papillo-edema was at its height. It is very logical to assume in this case that a destruction of the corpora quadrigemina did not cause blindness, but that blindness was accidental, being caused by an atrophy of the optic nerve, following papillo-edema. When the external geniculate bodies, however, are involved in the destructive process, we may have either hemianopsia or total blindness.

(b) *Pupillary Reaction*.—The centers for the iris are supposed to lie in advance of the nucleus of the third nerve. Therefore, unless the tumor is in the advance of the corpora quadrigemina, the light reaction will not be affected (Posey and Spiller,<sup>53</sup> Bristowe, Sachs).

In our case, it was found that the pupils at first responded to light; although when the author examined them later, light reaction was lost, but this was undoubtedly caused by the atrophy of the optic nerves. Bach, however, concludes that bilateral destruction of the corpora quadrigemina causes bilateral loss of pupillary light reflex. Unilateral destruction causes loss of light reflex of the pupil of the same side.

(c) *Hearing*.—We will next take up the subject of the relation between hearing and the posterior corpora quadrigemina. We have seen from the clinical examination of our case that hearing was unimpaired, even up to the very last. A careful examination, both for air and bone conduction, was made, but no defect of hearing was found. The

pathological report states that the posterior corpora quadrigemina were completely destroyed, and that the termination of the lateral fillet was in position to be injured. Clinical and pathological reports on this point are contradictory.

The experiments of Kallischer<sup>54</sup> on trained dogs would indicate not only that the dogs can hear, but that they can differentiate between tones, even though the posterior quadrigemina are destroyed. These experiments were repeated and the conclusions affirmed by Rothmann,<sup>55</sup> viz., that the posterior corpora quadrigemina can be destroyed without causing central deafness. Rothmann, however, found that there is some relation between the posterior quadrigemina and the sense of hearing, but that its importance is secondary to the internal geniculate body, and that when the posterior corpora quadrigemina are destroyed, its function is capable of compensation. Bach<sup>56</sup> states as a result of a clinical and pathological analysis that central deafness seems to result from a destruction of the posterior corpora quadrigemina, and that the destruction of one is followed by deafness of the opposite side.

Weinland (quoted by M. Allen Starr<sup>57</sup>) made a collection of 27 cases of lesions of the posterior corpora quadrigemina. In 13 cases deafness was noted, but in all these cases the lateral lemniscus was affected. In some cases there was bilateral deafness, in others the deafness was on the side opposite the lesion. Weinland, upon the evidence of his own case, as well as that of Ruel and Ferrier, comes to the conclusions that unilateral destruction of one posterior corpora quadrigemina and the lateral lemniscus leads to deafness of the opposite ear. In the other 14 cases the lesion did not reach the lateral lemniscus or there was no mention made of disturbance of hearing.

Oppenheim<sup>58</sup> quotes Seibman, who holds that disturbances of hearing result from lesions either of the lateral lemniscus or the posterior corpora quadrigemina.

The accepted course of auditory impulses (Held, Thomas, Van Gehuchten) is to the acoustic centers in the pons, thence along the lateral fillet and the posterior quadrigemina to the internal geniculate body, and thence to the cortex of the temporal lobe. In our case this tract was interrupted by a destructive lesion, destroying the corpora quadrigemina and the ending of the lateral fillet, and still hearing was intact. There are not many cases of this kind on record. In none of W. Nissen's eight cases was hearing involved at all.

In commenting on these cases Nissen expresses the view "that the corpora quadrigemina may be a reflex area in which the acoustic system is connected with the nuclei for ocular movements."

In Collins'<sup>59</sup> case hearing was normal. Similar cases have been put on record by Gordinier and Bielschowsky, but in these cases, while the posterior corpora quadrigemina were destroyed, the lateral fillet was not affected.

Our case is a clinical confirmation of the animal experiments of Kallischer and Rothmann, that destruction of the corpora quadrigemina does not lead to deafness.

We can conclude from the critical analysis of this case that neither blindness, deafness nor ataxia is pathognomonic of a disturbed function of the corpora quadrigemina. Nissen<sup>60</sup> has voiced this opinion before, and Marburg<sup>61</sup> has said more recently that hardly any focal symptoms are due to a destruction of the corpora quadrigemina.

Now, while this may be true in a physiological sense, from a clinical diagnostic standpoint it is not a good policy to circumscribe the corpora quadrigemina so closely. We must recognize from a practical standpoint that no tumor is going to be strictly localized to the corpora quadrigemina, but that tumors do originate here and eventually invade and compress the surrounding territory; and that, although external eye palsies, disturbances of vision, hearing and ataxia are neighborhood symptoms, they form so characteristic a syndrome, and thereby enable us to make so accurate a localizing diagnosis that we can rule out tumors originating from other parts, viz., the cerebellum. The practical importance of this conclusion is that we will, in case we can localize a neoplasm in the corpora quadrigemina, not subject our patients to futile, and perhaps fatal, exploratory operations. This does not, however, rule out decompression operations, which the author believes should be subtemporal rather than suboccipital; because the increased intracranial pressure in these cases is due to the development of internal hydrocephalus caused by the compression or occlusion of the canal of Sylvius.

(d) *Neighborhood Symptoms.*—The chief characteristic, therefore, of corpora quadrigemina syndrome is due to the neighborhood symptoms. Underneath the corpora quadrigemina are the nuclei of the third nerve; still deeper is the nucleus ruber, a cross-section of the frontopontine cerebellar tract, which is a crossed tract; deeper still are the peduncles. This juxtaposition of very important physiological tracts and centers has given rise to the symptom-complex of Benedikt. This syndrome consists of a paralysis of the third nerve on one side and of a paretic condition of the opposite arm and leg with tremor and ataxia. The Benedikt symptom-complex is more characteristic for vascular lesions, and it would be difficult for a tumor of the corpora quadrigemina to develop in a strictly one-sided way so as to produce the above symptom-complex. Both tumors of the corpora quadrigemina and of the cerebellum produce nuclear eye palsies and cerebellar ataxia. When seen late it may be difficult to localize the growth accurately. It is, however, accepted (Bruns, Spiller, Cushing<sup>62</sup>) that, where the history shows that the eye palsies preceded the ataxia, the growth is probably in the brain stem; but if the ataxia is the first symptom, the tumor is probably in the vermis-form lobe of the cerebellum, and compresses secondarily the corpora quadrigemina. In the tumor described by the author, where the growth began in the corpora quadrigemina, the ataxia was practically the last of the symptoms to develop in a chronological order; in fact, both the external eye palsies and the blindness had been in existence for a year before the ataxia developed. Nothnagel's teaching is to the contrary: viz., one of the functions of the corpora quadrigemina is the power of muscular coördination.

*Tumors of the Pons.*—From a therapeutic standpoint it is very important to draw a sharp line between tumors originating in the pons and tumors of the cerebellopontine angle and of the lateral lobes of the cerebellum. The latter two locations offer very favorable fields for surgery; whereas, in the former, surgical interference is absolutely contra-indicated.

The chief characteristic of tumors of the pons is that the syndrome of paralysis alternans is developed in a general way over a period of time extending over some months, while simultaneously the patient shows signs of increased intracranial pressure. All possible combinations of crossed paralysis can be encountered, depending upon the region in which the tumor has its origin. Sooner or later, however, the tumor



FIG. 19.—LARGE GLIOMA OF THE PONS.

involves both sides of the pons. Even then we can trace, both in the chronological order of development and in the predominance of signs, a crossed arrangement: cranial nerves first and predominantly affected on one side; the arms and legs affected with paresis; ataxia and sensory disturbances on the opposite side (Fig. 19). This condition is best illustrated by a typical case:

C. W., aged 12, school girl. (Fig. 20.) Family history was negative. There was no tuberculosis in the immediate family. Patient was well up to four months ago. Onset of trouble was marked by a slight defect in the right eye; patient saw double; at times had some fever; headache occasionally at first, later more frequently, and, just previous to the time she was first seen, had attacks of vertigo, and had staggered; had vomited every morning. No defect of hearing.

*Examination:* At the time of examination the mental condition was



normal. Pupils equal and responded to light, optic disks normal; there was paralysis of both internal and both external recti muscles; the eyes could be moved upward and downward; paralysis of the right facial, both upper and lower branches; right eye could not be closed. The tongue deviated to left. Arms were normal in all respects. In the right leg the patellar reflex was practically abolished, left patellar reflex exaggerated; left ankle clonus, bilateral Babinski sign; no weak-



FIG. 20.—PARALYSIS OF RIGHT EXTERNAL RECTUS, RIGHT FACIAL AND LEFT-SIDED HEMIATAXIA.

ness in legs. Hearing normal. When eyes were closed, patient walked with a staggering gait, with a tendency to fall toward the left. There was no static ataxia, no ataxia in recumbent position.

*Course of Disease:* Two weeks later the condition was unchanged, but a horizontal nystagmus had been developed, on looking to right. After four weeks there developed an ataxia of both arms, without any loss of muscular power. With blindfolded eyes patient could not walk forward at all, but invariably was forced toward the left; she staggered to left when walking, and fell to left in Romberg test. Hearing had become defective in the right ear, both for bone and air conduction. Papillæ remained normal; left eye movement upward somewhat dimin-

ished. Left patellar reflex had returned, and both were now exaggerated.

On May 24, 1910, mental condition was good, optic disks normal, eye muscles as before, paresis of soft palate, patient choked on swallowing. Right side of face remained unchanged, no loss of sensation anywhere, no areflexia cornea. Speech was difficult, dysarthria was present. Patient developed some weakness, and a very acute ataxia of the left side, both arm and leg, and patient was unable to walk without assistance on account of the left-sided ataxia. Ankle clonus was present on the left side with exaggerated patellar reflexes. Adiadokokinesia of the left arm was marked.

This case presented the typical history of an infiltrating tumor of the pons. The damage wrought was caused by a gradual destruction of the various nuclei and structures of the pons, partly by invasion, partly by compression.

The symptoms are chiefly bilateral: viz., bilateral involvement of the eyes, bilateral ataxia of the arms, bilateral increase of the patellar reflexes; but the involvement of the seventh and eighth on the right side, paresis of the left leg, with ankle clonus on the left side and ataxia of left arm and leg later on, show the typical condition of pontine and medullary growths, viz., paralysis alterans.

The eye-muscle palsy is due usually to an involvement of the posterior longitudinal bundle. According to Spiller, this produces usually a paralysis of the lateral association movements so that the paralysis of the associated ocular movements is toward the side of the tumor.

Oppenheim thinks that an early loss of the corneal reflex is rather indicative of pontine tumors.

A tumor of the pons (see Figs. 11-12) may be so small as to cause no general signs, and merely a one-sided, slowly progressive hemiplegia, as occurred in this case.

*Tumors of the Cerebellopontine Angle.*—Tumors in this locality have assumed quite an importance in recent years on account of the success attending their surgical removal (see Fig. 7).

The typical tumor here is of very slow growth, usually a fibroma or endothelioma, growing from the trunk of the auditory nerve, but the seventh and fifth may also be the seat of origin. The typical early syndrome is that of defective hearing on one side, gradually increasing, with occasional attacks of vertigo, with loud noises and ringing in the ear; then the general symptoms of headache, vomiting, vertigo, unsteady gait, plus more or less pronounced involvement of the fifth, sixth, seventh and eighth cranial nerves, on one side, with perhaps an indication of ataxia of arm or leg on the same side; and finally, signs and symptoms which point to a compression of the medulla and pons. This syndrome is so typical that in the majority of cases the localizing diagnosis is easy.

We cannot give a better or more concise grouping of signs and symptoms than by quoting M. Allen Starr.<sup>63</sup>

*"Symptoms of Tumors of the Acoustic Nerve.*—The symptoms which indicate the location of a tumor in the cerebellopontine angle upon the acoustic nerve may be divided into three classes: (1) those referable to the cranial nerves; (2) those referable to the involvement of the cerebellar peduncles; and (3) those referable to compression of the tracts passing through the pons.

*"(1) Symptoms Referable to the Cranial Nerves.*

*"(a)* Slight anesthesia of the face on the side of the tumor, first shown by corneal anesthesia and by absence of the corneal reflex.

*"(b)* Weakness of the external rectus muscle of the eye on the side of the tumor, due to a pressure on the sixth nerve. This may first be noticed by the occurrence of nystagmus on turning the eyes toward the tumor, and later a decided internal strabismus may occur. The eye looks away from the tumor.

*"(c)* A weakness of the muscles of the face on the side of the tumor, first noticeable in a slight disturbance of the act of winking and a slight lack of expression, which is later followed by an actual weakness of all the muscles supplied by the seventh nerve. Pressure on this nerve is rarely, if ever, sufficient, however, to cause a reaction of degeneration in these muscles.

*"Cushing* has published a very rare case in which facial spasms, simulating jacksonian epilepsy, preceded the other tumor symptoms for a year.

*"(d)* Tinnitus in the ear on the side of the tumor, soon followed by some deafness in the ear, which may be slight and only detected by tests with the Galton whistle, high notes or low notes, or both, being lost. This deafness may be as marked for bone conduction as for air conduction.

*"(e)* Vertigo, felt by the patient as a sensation of falling toward one side, or as a sensation of rotary movement of the body, both of which symptoms must be ascribed to irritation of the labyrinthine division of the auditory nerve.\*

*"(f)* Difficulty of swallowing and hoarseness of the voice, owing to pressure on the ninth nerve.

*"(g)* Sudden attacks, which may be called vagus attacks, referable to irritation of the tenth nerve, consisting of rapid pulse, sensations of flushing of the body or of the head, sudden faintness without an actual loss of consciousness, attended by more or less vertigo.

*"(h)* Paralysis of the tongue, shown by thickness of speech or difficulty of articulation, and by protrusion of the tongue toward the side of the tumor.

\* "M. Allen Starr, *Brain*, 1904, 525.

"I cannot confirm the statement of Stewart and Holmes, that in cerebellar tumors the sense of displacement of objects in front of the patient is from the side of the lesion to the opposite side. They also state that when a tumor is within the cerebellum the subjective rotation of self is from the side of the lesion toward the healthy side, but when the tumor is outside the cerebellum the subjective rotation is from the healthy side toward the side of the lesion. Oppenheim has also failed to confirm this assertion."

“(2) *Symptoms Referable to the Involvement of the Cerebellar Peduncles.*—The second set of symptoms is referable to the compression of the cerebellar hemisphere and its peduncles. The portion of the cerebellum that will necessarily be involved is the flocculus, which projects over the middle peduncle of the cerebellum as it comes from the pons. As we have no means of distinguishing between the functions of different portions of the cerebellum, it is uncertain whether the symptoms of a cerebellar nature are due to destruction of this flocculus or of the two peduncles entering the cerebellum just under the site of the tumor. These symptoms are:

“(a) A staggering gait and feeling of uncertainty of the position of the body in space when supported upon the legs, which causes swaying when the eyes are closed and staggering when the eyes are open, attended by a disagreeable sense of vertigo, which leads the patient to seek support whenever in a standing posture. The direction of the staggering is, in the majority of instances, away from the tumor, although cases have been put on record in which the patient staggered toward the side of the tumor. The direction of the staggering is not to be taken in itself as a very important symptom, but the fact that the patient staggers uniformly toward one side is an important symptom of an affection of the peduncles of the cerebellum as they enter the organ. The existence of staggering, therefore, in a definite direction, combined with evidences of the implication of the cranial nerves upon one side, is a definite local sign of a tumor in the cerebellopontine angle.

“(b) Another symptom of cerebellar origin is an imperfect muscular tone in the muscles of the arm and leg on the side of the tumor. This lack of tone is attended by an awkwardness of movement, not due to any actual weakness, but to an imperfect coördination of the motions performed. There may be also an ataxia of the leg, so that to stand on one foot is impossible. Such an ataxia in the leg may lead to staggering toward the side of the tumor. The maintenance of a proper tone in the muscles appears to have some relation to the response of those muscles to irritation. It is probably on this account that lesions of the cerebellar peduncles or of the cerebellum are usually attended by a loss of knee-jerk and of the deep reflexes on the side of the lesion; yet this symptom of a loss of reflex on the side of the tumor is not always found in these cases of pontine angular growth. It has been observed, however, in too many cases to allow us to overlook it.

“(3) *Symptoms Referable to Compression of the Tracts Passing through the Pons.*—A third set of symptoms is to be traced to a compression of the motor tracts and sensory tracts passing through the pons and medulla on their way to and from the limbs of the opposite side. Compression of the pons is less likely to cause disturbance in the transmission of sensation than in the transmission of motor impulses. Weakness, therefore, of a hemiplegic type in the arm and the leg on

the side opposite to the tumor is more commonly observed than is anesthesia in the corresponding parts. This weakness is usually attended by an exaggeration of the reflexes, by an increase in the knee-jerk, ankle clonus, and of the loss of the knee-jerk upon the side corresponding to the tumor. This weakness of one leg may intensify the difficulty of walking and may markedly influence the gait. A patient with a weak leg has something of a tendency to stagger toward the leg that is weak, to use it less freely, and to bend downward toward that side. It has been already remarked that many of these patients stagger away from the tumor, and it is not at all impossible that this direction of the



FIG. 21.—BASE OF THE BRAIN. (After Campbell.)

staggering is due to the imperfect use of the leg on the side opposite to the tumor. The actual weakness present in the arm or leg may be easily detected by dynamometer tests, and in many cases has amounted to such a marked hemiplegia that any use of the arm or of the leg was impossible. While anesthesia and analgesia in the limbs of the side opposite to the tumor is much less commonly observed than is paralysis, many patients complain of feelings of numbness, tingling, gooseflesh, or burning in these limbs, and such paresthesias may be followed by an actual disturbance of sensation. In the advanced stages of these cases, in which the patients have died of the tumor, a hemiplegia has developed toward the close of life, not, however, involving the face. It is in these extreme cases that anesthesia has been observed in the paralyzed limbs."

We cannot lay too much stress on the importance of *early diagnosis*

of tumors of the cerebellopontine angle. They are very amenable to surgical treatment, as the numerous cases on record testify; but when the case has advanced to the point of compression of the pons, little is to be hoped for from surgical interference. The aurist should be the first to recognize these cases, because of the early involvement of hearing. He should be on the lookout for the early symptoms: viz., progressive loss of hearing with middle ear normal, vestibular attacks of vertigo, slight weakness of face and areflexia cornea on the same side, with perhaps weakness of external rectus of same eye. No other focal lesion, with the possible exception of basilar syphilis, produces this syndrome.

From a standpoint of *differential diagnosis*, we may say that tumors of the cerebellopontine angle show an early predominance of unilateral focal signs in the fifth, sixth, seventh and eighth nerves, whereas tumors of the pons and medulla show bilateral focal signs with a clear indication of hemiplegia alternate. In both, the focal signs may precede the general signs of brain tumor, and frequently do. Pons and medulla tumors, being small, produce less marked general signs of brain tumor; whereas, the angle tumors have later on marked general signs. Choked disk is characterized by its absence in pons tumors, although this is not invariably the rule; whereas, the cerebellopontine angle tumors manifest general signs. Choked disk is almost invariably present, together with headache, vomiting and vertigo, partly due to an associated internal hydrocephalus.

Oppenheim's triad of signs may be seen early: viz., disturbance of hearing; paralysis of winking; and a diminished corneal reflex.

*Tumors of the Cerebellum* (Fig. 21).—An *early diagnosis* of cerebellar tumors is very desirable from a surgical standpoint. When these tumors and cysts have grown to such a size so as to compress the cranial nerves and the pons itself (Fig. 22), the diagnosis is not difficult, but the surgical prognosis is bad; whereas, the outlook is good if an early localizing diagnosis can be made before the tumor has grown beyond the confines of the cerebellum. This early diagnosis is very difficult. Not only is it difficult to say whether the growth is located on one side or the other in the hemisphere; but it is often difficult to rule out the growths of the frontal lobe, or to say with certainty whether the symptom-complex is caused by a tumor, by acquired internal hydrocephalus, or whether we are dealing with the so-called pseudo-tumor symptom-complex.

The chief interest in the study of the differential topographic diagnosis of tumors below the tentorium cerebelli is whether we have arrived at that state of diagnostic acumen which will enable us to say with any degree of certainty whether a growth is located in the cerebellum itself, and if so, and above all, which lobe of the cerebellum is involved. The writer believes that we can say with some accuracy whether a growth is in the pons or in the region of the corpora quadrigemina, and that the diagnosis of growths in the cerebellopontine angle can be made with almost equal facility; but the greatest stumbling block is offered

by tumors of the cerebellum itself. We have seen what signs and symptoms are peculiar to neoplasms of the pons, of the region of the corpora quadrigemina and of the cerebellopontine angle. Let us now go on.

In arriving at a diagnosis of tumors of the cerebellar hemisphere, our first step is one of exclusion; we must exclude tumors in the above-mentioned locations. Then we must exclude frontal lobe tumors. We cannot here go into the symptomatology of frontal lobe tumors, but suffice it to say, that there are well known physiologic facts and clinical and surgical experiences which prove that at times it is practically impossible to say whether the tumor is in the frontal lobe or in the cerebellum.



FIG. 22.—LARGE TUMOR OF THE CEREBELLUM.

The physiologic fact to which the author refers is that in animal experiments the loss or disturbance of function of one cerebellar hemisphere when removed, especially the ataxia, quickly disappears after the operation; but if the animal is then deprived of the opposite frontal lobe, all the cerebellar symptoms return. In a word, the frontal lobe in a measure takes up, or at least compensates for, the loss of the function of the crossed cerebellar hemisphere. This interaction of function takes place through the frontopontine cerebellar tract. It is also a well-known fact that tumors of the frontal lobe, both by causing ataxia and by producing distance pressure signs, can cause a symptom-complex which at times can hardly be distinguished from a cerebellar symptom-complex. Moreover, it is not unusual to have unilateral spasms and even jacksonian seizures in cerebellar lesions, as the cases of Mills, Weisen-

berg<sup>64</sup> and Hoppe<sup>65</sup> show. We are gradually, however, improving our knowledge of frontal growths, as well as of those of the cerebellum. We shall probably make fewer mistakes along these lines if we pay greater attention to the chronologic order of the development of signs and symptoms. For it is the author's theory that in frontal growths some change in the mental state will occur, and often antedate the general symptoms of brain tumor; whereas, in cerebellar tumors, mental symptoms, if they occur at all, manifest themselves late. In the last two cases of frontal tumors in the writer's observation the mental deterioration was most manifest, one of the patients at times even becoming maniacal, and having been brought into the hospital in this condition.

In making the diagnosis of cerebellar growths, we must also rule out pseudo-tumors of the brain, a subject which has been placed on record by Nonne, Oppenheim, myself and others. This pseudo-tumor symptom-complex is more apt to resemble the cerebellar symptom-complex than any other. Its pathology is unknown. The autopsy in one of the writer's cases was entirely negative in regard to the brain. Here is a summary of the typical syndrome: headache, violent vertigo, vomiting, bilateral choked disk, paresis of the external recti muscles of the eyes, areflexia cornea, especially of the right eye; tinnitus, with diminished hearing on the same side, cerebellar ataxia and deflection of head and even entire body to one side. These signs of pseudo-tumor are in a manner similar to acquired, internal hydrocephalus or serous meningitis. These two conditions must be ruled out; and the only means at our command are the presence of other signs and symptoms, which are present in cerebellar cases, and absent in the above symptom-complexes. On these signs we shall presently lay stress.

A few words on the *physiology* of the cerebellum will be in place here. The chief function of the cerebellum as ascertained by animal experimentation is that of automatic coördination. Through the medium of the cerebellar tract, Gowers' tract, and the vestibular nerve, all of which, Bruce holds, end in the cortex of the vermiciform lobe, we ascertain the state of contraction, and the tone of all muscles of the body and the position of the body. When these tracts are interfered with within the cerebellum we have the chief symptom of cerebellar disease, viz., cerebellar ataxia. Lesions of the cerebellum, however, are not the only factor in the production of cerebellar ataxia. We know that tracts lead from the cerebellum to the pons, through the corpora quadrigemina and to the opposite cerebral hemisphere, and that the destruction of any one of these tracts will cause cerebellar ataxia. Hence, lesions of the frontal lobe, of the corpora quadrigemina and of the pons may cause cerebellar ataxia. In the lesions of the cerebellum, however, we have ataxia without any associated signs, such as form part of the syndrome in the lesions of the frontal lobe, of the corpora quadrigemina and of the pons. In considering cerebellar ataxia and other signs of cerebellar lesions we must not forget that the loss of function of one cerebellar hemisphere, as Munk and others have shown, may be compensated by the opposite frontal lobe, and that symptoms may disappear, or that disease of one



hemisphere may even run a latent course. Babinski lays much stress on a physiologic phenomenon which Munk attributes to the cerebellum, viz., a harmonious interaction between the movements of the extremities and those of the trunk. Babinski<sup>66</sup> calls this function "synergie," and the loss of this function "asynergie cerebelleuse." By this is meant a loss of harmony, which, for instance, may show itself when walking, by an attempt to bring the leg forward, while the trunk does not change its position, or may even go backward. Asynergie cerebelleuse may be confined to one side—hemiasynergie—and Babinski says that it points to a lesion of the cerebellar hemisphere on that side, or to one of the tracts leading to the hemisphere, or from the hemisphere on that side. Oppenheim<sup>68</sup> seems to agree to this; Spiller<sup>67</sup> dissents. Forced movements are seen in animals and rolling movements; Munk, however, does not attribute these to lesions of the cerebellum, but to other causes. In the human being we see a tendency to assume certain positions in bed, or to hold the head to one side, the diagnostic value of which we will consider later.

Astasia-abasia, hemiataxic movements, homolateral weakness of muscles, and homolateral convulsions will be considered as localizing signs later on, as will also speech disturbances and nystagmus, all of which have been attributed to loss of function of the cerebellum.

I. *Focal Signs*.—What are the focal signs which clinical experience has taught us point to tumors of the cerebellum? The following syndrome calls for analysis:

(1) Cerebellar ataxia; (2) ataxic movements, hemiataxia, asynergie cerebelleuse, hemiasynergie and tremor; (3) vertigo; (4) nystagmic jerking and other eye-muscle signs; (5) atonic paresis of trunk and extremity muscles on one side; (6) adiadokokinesia and speech disturbances; (7) convulsions, unilateral or bilateral; (8) attitude of the head.

Let us take up the signs and symptoms in the order as they are given:

(1) *Cerebellar Ataxia*.—The typical reeling, staggering gait is probably seen only in tumors of the vermiform lobe, and perhaps also in quadrigemina tumors; but here it will be associated with extensive eye-palsies, which will be absent in the cerebellar lesion.

What is more commonly seen is staggering to one side and a tendency to fall to one side. The author believes that this, when unassociated with pontine signs or symptoms, may be looked on as fairly characteristic of lesions of the cerebellar hemisphere. It would be of great value to prove, if it could be established as a law, that the patient reels or falls to the side of the lesion. Weisenberg seems to think that this is the case. Two of my patients showed a tendency to fall toward the side of the lesion; one did not. Oppenheim,<sup>68</sup> Siemerling<sup>69</sup> and Spiller hold that we cannot rely on this sign as pointing to the side of the lesion. Siemerling says that cerebellar ataxia may be entirely absent. If the vermis is the seat of the growth, the ataxia may be so great that the patient is unable to stand at all. This is true likewise of growths of the corpora quadrigemina; but in advanced stages it may be present, too,

in tumors in or those pressing on the lateral lobes, or in tumors of the brain stem. This may be explained by distal or contiguous pressure on the vermiform lobe or cerebellar tracts.

(2) *Hemiataxia and Hemiasynergy*.—These, which Oppenheim thinks may be identical manifestations of cerebellar incoördination, are often present, and may, after further investigation, be found to be of great topographic diagnostic importance as pointing to lesions in the same side of the cerebellum.

Bruns<sup>70</sup> says that hemiataxia is a valuable sign, because it occurs early, and is a sign of an intracerebellar lesion. In the four cases reported by him it occurred in the homolateral arm in each case.

Soques<sup>71</sup> reports hemiasynergy and adiadokokinesia on the same side, homolateral, in a case of tumor of the cerebellopontine angle.

In one of the writer's cases there was static ataxia of the right leg (side of cyst), before the operation, loss of patellar reflexes and atony of both legs, but no loss of muscular power. The ataxia became so marked that the patient refused to attempt to walk. After the operation the ataxia of the left arm and leg became very acute. In a word, the cyst was found on the left side; and the ataxia was most marked on the left side, the right arm and leg being free. When ataxia is suspected but not present in the ordinary way of standing or walking, Oppenheim recommends that the patient be placed in the ordinary Romberg position, and be asked to bend forward with closed eyes. As a rule, not only will the loss of equilibrium show itself, but also the side toward which the patient sways will be of consequence. Some stress has been laid on unilateral tremor, similar to that of multiple sclerosis, as a sign of cerebellar disease. Collins,<sup>72</sup> Bruns, Siemerling and Oppenheim have called attention to this sign, and when present, it is usually homolateral.

(3) *Vertigo*.—This, which is invariably present in subtentorial growths, is not of much localizing value. The exact differentiation between vertigo of intra- and extracerebellar origin, as defined by Stewart and Holmes, has not been verified by others and needs further investigation: namely, that in intracerebellar tumors the objects and the apparent movements of their own bodies are from the side of the lesion to the opposite side, and in extracerebellar tumors the apparent movement is toward the side of the lesion. If, however, vertigo is brought about by changing the position of the body or of the head, we may safely say that this occurs when the body or the head is turned away from the side of the lesion.

(4) *Nystagmus*.—Not the typical nystagmus seen in multiple sclerosis, but a nystagmic jerking, when the eyes are turned to one side or the other, is frequently seen in subtentorial growths. Munk<sup>73</sup> says that strabismus and nystagmus are not seen in animals as a result of the removal of one-half of the cerebellum, but as a result of injuries to the neighboring parts. Siemerling, although admitting it is a sign of intracerebellar lesion, thinks that it is caused by pressure on the pons or corpora quadrigemina. H. Neuman<sup>74</sup> and Collins look on it as a cerebellar

sign. Nystagmic jerking is usually seen when the eyes are turned toward the side of the lesion, but this is not the invariable rule. It was present in one of our cases toward the side of the lesion. It was not present, either before or after the operation, in two other cases.

Spiller, in a case of cerebellar abscess, says that the nystagmus became more marked when the patient looked toward the seat of the lesion. H. Neuman has confirmed this in a later communication.

Siemerling does not feel that the direction of the nystagmus has a positive localizing value, while Oppenheim thinks that nystagmus may be a sign on intracerebellar disease, although it more frequently is the result of distal pressure. The author has never seen general ataxia of the eyeballs such as Spiller and Weisenberg describe in a subtentorial tumor, but has seen it in a case of nuclear degeneration of the centers in a case of chronic bulbar palsy.

In this respect, we call attention to the fact that the position of the head and the position of the body have a marked influence on bringing out signs of cerebellar tumors that may be latent. Oppenheim in a recent article gives his experiences on this subject. He cites two cases of tumor of the cerebellum, in which a nystagmus was only slightly indicated when the patients, in a standing position, looked to one side or the other, but which became very marked, even when the eyes were at rest, if the patients reclined on one side. In another case in which nystagmus was absent with the patient standing or lying on the back, if the patient lay on his right side and looked toward the left, nystagmus appeared at once, and a paresis of the external rectus became apparent. In another case, nystagmus on looking toward the side of the lesion appeared only after the patient had been turned on a revolving chair two or three times. In two other cases of subtentorial tumors, areflexia cornea was produced by having the patient lie on the side opposite to the tumor.

(5) *Atonic Paresis*.—Atony of the trunk muscles on the side of the lesion, homolateral weakness in the ataxic limb and loss of patellar reflexes on one side or both, may occur. Bruns says that it occurs only in acute cases, after removal of a part of the cerebellum. Siemerling says that it is still a debatable sign.

(6) *Adiadokokinesia*.—Probably one of the most valuable signs which will indicate the side of the lesion is one to which Babinski has called attention, namely, adiadokokinesia. By this is meant a slowing of movements of an alternating character; it is best illustrated by successive pronation and supination of hand and forearm. In lesions of the cerebellar hemispheres there is a marked diminution in the rapidity with which these movements can be alternated, and it occurs always on the homolateral side.

Adiadokokinesia, according to Bonnhöffer,<sup>75</sup> who describes speech disturbance in a case of cerebellar tumor, may manifest itself as bradyphasia. He says that it is due to an inability of the patient to rearrange his lip and tongue muscles rapidly, which is necessary for fluent speech. Other speech disturbances have been ascribed to cerebellar lesions, as a

staccato, jerky mode of talking, which has been attributed to inco-ordination or ataxia of the muscles of tongue, lip and larynx. Speech becomes slow, repetition of long words causes a chopped-off reproduction, and at times stumbling and stammering. Rapid speech is impossible, but there is no anarthria.

(7) *Convulsions*.—General convulsions or unilateral convulsions of the cerebellar type, viz., opisthotonos, momentary loss of consciousness with a general clonic spasm of very short duration, are indicative of subtentorial pressure and irritation of the pons, rather than of intracerebellar tumor.

(8) *Attitude of the Head*.—The attitude of the head may give us some indication as to the side of the lesion. Batten called attention to the fact that the head is inclined in such a way that the occiput points to the side of the tumor, and the chin is pointed away from that side. Collins, in a case of hemorrhage, describes just the opposite condition. Oppenheim says that there is no rule, but that the patient assumes such a position of the head and body as cause him least inconvenience. Spiller also thinks that there is no rule. Sholz has used the Neisser puncture test to determine the side of lesion, and located the tumor in two out of three cases by this means. Oppenheim calls attention to a difference in the percussion note on the two sides, and says that we may find more dullness on the side of the lesion. Bruns calls attention, especially in children, to tenderness on percussion, and the cracked-pot sign, on the side of the lesion.

The focal symptoms which have been described above are produced by tumors which grow in the hemisphere of the cerebellum. If the growth is large and projects beyond the confines of the cerebellum, it will compress the cranial nerves, and later on the pons itself. We then have symptoms on part of the fifth, sixth, seventh and eighth nerves on one side with contralateral spastic weakness, sensory disturbances, ataxia of the opposite extremities. Oppenheim describes a large tumor of the cerebellum which by compression produced symptoms on part of the occipital lobe.

II. *Acute General Symptoms*.—Cerebellar tumors produce some very acute general symptoms. The headaches are very acute, choked disks occur early and are very extreme, and are apt to pass quickly into the atrophic stage. Some of the cases show very acute attacks of vomiting of the typical projectile type without nausea. A patient may vomit during a meal and begin to eat at once after the vomiting has ceased. Sometimes the turning of the head to one side will cause vomiting.

*The Bárány Tests and Tumors of the Posterior Fossa*.—There is undoubted value in the Bárány tests for differentiating between lesions of the labyrinth and tumors of the cerebellum, pons, medulla, and cerebellopontine angle. These findings are, however, only of supplementary value and for accurate localization must be considered in connection with the other signs and symptoms present.

The fact that the findings are at times ambiguous and contradictory to the anatomical lesions found may be due, as we shall see, to the fact

that the horizontal and vertical canals were not separately examined. The following summary seems to be justified on observations to date:

(a) *Vertigo*.—An individual with normal labyrinths will experience vertigo when turned in a revolving chair. The absence of vertigo under the turning test, with normal labyrinths, will point to a disease of the medulla, pons or cerebellum. B. Alex. Randall and Isaac H. Jones<sup>76</sup> say that the ear stimulus which produces vertigo passes by way of the vestibular portion of the eighth nerve to Deiters' nucleus; those from the horizontal canals pass through the medulla and thence through the inferior cerebellar peduncle to the cerebellum; and those from the vertical canals pass by way of the pons through the middle peduncle to the cerebellum, and through the superior peduncle to the cerebrum.

The absence of vertigo on the turning test with normal labyrinths indicates a lesion of either medulla, pons, cerebellum, peduncles, or internal hydrocephalus which can exert pressure on the floor of the fourth ventricle. In order to more accurately locate the lesion, the other symptoms and signs present must be properly evaluated.

(b) *Past-pointing*.—Spontaneous past-pointing, like spontaneous nystagmus, is often a symptom of cerebellar or pontine disease.

In the Bárány test, past-pointing follows the same rules as vertigo. Absence of past-pointing with normal labyrinths points to a disease or tumor in the above-mentioned localities of the posterior fossa.

(c) *Nystagmus*.—Neuman believes that the cerebellum has an inhibitory effect on the nystagmus directed toward its own side: that, therefore, in an organic disease of the cerebellum, this inhibition is lost; and that therefore in the Bárány test, in tumors or organic disease of the cerebellum, the duration of the nystagmus toward the side of the lesion is increased; and that this so-called enduring nystagmus may last, instead of 21-22 seconds, 5-15 seconds longer.

The majority of observations, however, have been that the nystagmus is diminished or absent altogether when the test is applied to the ear on the side of the lesion.

Ernest G. Grey,<sup>77</sup> after an analysis and study of 31 cases, confirms in a general way the above findings, and quotes Bárány. He says that most cases of brain tumor in the posterior fossa with considerably increased intracranial pressure experienced very little discomfort from the caloric tests and that much dizziness, nausea and vomiting in response to these caloric tests speak against a process in the posterior fossa.

*Caloric Tests*.—What holds for the turning tests also holds for the caloric tests. We need not, therefore, repeat the above statements.

Randall and Jones believe that interruption of the impulses from the vertical canals are produced by tumors of the cerebellopontine angle and by internal hydrocephalus, and that interruptions of impulses from the horizontal canals are produced by tumors or lesions of the medulla and cerebellum. They also believe that the vestibular branches go to the opposite hemisphere of the cerebellum.

Further investigation, however, is necessary before absolute finalities can be concluded on some of the above points.

*Tumors of the Fourth Ventricle.*—These may be echinococcus cysts, or they may be solid tumors (Fig. 23). They often give rise to no symptoms at all; or they may cause those of internal hydrocephalus. In other cases, there is a gradual compression of the middle lobe of the cerebellum giving rise to a staggering gait.

The tumor may grow in such manner, as shown in the illustration, as to cause a gradual compression of the floor of the fourth ventricle and, later on, the deeper structures of the pons and medulla. These tumors



FIG. 23.—TUMOR OF THE FOURTH VENTRICLE.

History and signs in case of fourth ventricle tumor. (Courtesy of Dr. Throckmorton.)

GENERAL SYMPTOMS: Headache, projectile vomiting, choked disk, vertigo.

CEREBELLAR SYMPTOMS: Right sided gait, ataxia (uninfluenced by closure of eyes), nystagmus, dysdiadokokinesia, asynergia, characteristic attitude of head, hypotonia of muscles of right arm and leg.

BRAIN STEM SYMPTOMS: *Right:* Ophthalmic division 5th, abducens, facial, auditory, glossopharyngeal, pneumogastric, spinal accessory, motor pathways to left arm and leg involved. *Left:* Abducens (slight), auditory (moderate), hypoglossal (?).

can hardly be differentiated from primary tumors of the pons, except that they may cause internal hydrocephalus. In this case the signs of increased intracranial pressure will be very marked, whereas in ordinary pons tumors these general symptoms are rarely ever present.

Bruns calls attention to the fact that a change of position in the patient may cause a sudden onset of the symptoms; he believes that this phenomenon is caused by unattached and movable cysticerci in the fourth ventricle.

Cushing lays stress upon suboccipital pain, a peculiar bowed position of the head, and periodic attacks of headache, vomiting and cervical rigidity, the fluctuation in the symptoms being due to the variations in the hydrocephalic pressure.

Polydipsia and polyuria as well as glycosuria are symptoms due to pressure on the floor of the fourth ventricle. Sudden death, with slow pulse and respiratory paralysis, is due to this same pressure. Choked disk occurs only secondarily and varies with the degree of internal hydrocephalus.

*Tumors of the Gasserian Ganglion.*—Ernest Sachs<sup>78</sup> was able to collect twenty-one cases in the literature, all but three occurring on the left side.

These cases are characterized by acute pain, usually beginning in one of the branches of the fifth and gradually extending until all three branches are involved. There is also a subjective loss of sensation and later on the motor branches of the fifth are affected.

W. B. Cadwalader,<sup>79</sup> basing his observation on nine cases, says that the most striking features of tumors of the gasserian ganglion are subjective and objective disturbances of sensation, sympathetic paralysis of the eye on the same side, third nerve palsies, disturbances of smell, unilateral disturbance of vision on the same side and ataxia. These signs may be followed by deafness, or deafness may not develop at all. The general signs of brain tumor are not well marked. Surgical intervention is usually not successful.

**BRAIN-TUMOR SYMPTOM-COMPLEX WITH TERMINATION IN RECOVERY: PSEUDO-BRAIN TUMOR.**—We are at times confronted with cases which present the general symptoms of a brain tumor, together with focal signs, which not only seem to render the general diagnosis of a cerebral neoplasm probable, but the focal signs are more or less marked, even to such an extent that we have little hesitation in designating the seat of the tumor. After a while, however, perhaps after several remissions and exacerbations extending over a period of years, these cases recover, showing, however, some defect, usually on the part of the eyes. Then death is caused by some other disease, and the brain is found perfectly normal.

Both the cases which recover and those in which a negative condition of the brain is found after death are of sufficient importance to merit our attention. While every one of us has undoubtedly seen cases of these kinds, the literature concerning them is exceedingly scanty. There are but two papers which deal extensively with this subject. These are the articles of Nonne and Oppenheim. Nonne's<sup>80</sup> article gives in detail 8 cases occurring in adults, and Oppenheim's<sup>81</sup> deals with a similar condition in children.

It is needless to say that cases such as these cannot be attributed to a functional derangement of the nervous system. We may as well rule out hysteria at once. Such an array of general and local symptoms can be due only to some organic change either in the brain itself or in its membranes, and this lesion must be capable of complete retrograde change, thereby restoring the brain to its original, normal condition.

In considering the possible pathological conditions underlying these cases we must divide them into two groups:

(1) Those cases in which death has occurred from some accidental cause and in which the autopsy revealed no brain lesion whatever.

(2) Those cases in which recovery occurred and the patients are still alive, or having died, no autopsy was held.

There are very few cases of the first group on record. Nonne publishes three cases of this kind with autopsy in which the brain examination, including microscopic and bacteriological examination, was entirely negative. The author<sup>65</sup> has published a series of these cases, one of which came to autopsy without showing any lesion to account for the symptoms during life. While Nonne declines to consider the possibility of hydrocephalus acquisitus or serous meningitis, but inclines to the theory that some unknown and hitherto undiscovered organic lesion which is perfectly curable must be looked upon as the cause of the trouble, it seems to the writer that we must consider one of the following conditions as the underlying cause. We refer to:

- (a) Serous meningitis producing acquired internal hydrocephalus;
- (b) Hemorrhagic non-purulent encephalitis with serous effusion;
- (c) Chlorosis;
- (d) Chronic cerebritis.

In the purely clinical cases, which have recovered after all the signs and symptoms of brain tumor were present, we must consider, in addition to the above conditions, the possibility of

(e) Brain tumors or tubercles which have either undergone a retrograde metamorphosis, or have become arrested in their development, and to which the brain has accommodated itself.

It has been shown that all of the above pathological conditions except cerebritis may produce a symptom-complex not unlike that of brain tumor and terminate in recovery.

(a) *Internal Hydrocephalus*.—Let us take up internal hydrocephalus first. First, there can be no doubt to-day that internal hydrocephalus or serous meningitis occurs quite frequently in the adult; and in the second place, it can hardly be doubted that although most of these cases terminate fatally, recovery may and does take place.

It is possible that the majority of cases with brain-tumor symptom-complex which terminate in recovery are really cases of serous meningitis of a subacute or chronic character, leading to internal hydrocephalus. We know now that acquired hydrocephalus not only produces the general signs of a brain tumor, such as headache, vomiting, vertigo and choked disk, but also focal signs, such as staggering gait, hemiplegia, aphasia and paralysis of the various cranial nerves.

Oppenheim calls attention to the fact that it is difficult, and often impossible, to differentiate between a tumor of the occipital fossa and meningitis serosa, and that the latter condition is the most frequent cause of a mistaken diagnosis of a cerebellar tumor. He says, further, that these cases usually occur in women who present the following symptom-complex: headache, vertigo, vomiting, choked disk, paresis of the external recti muscles, more especially of the right eye, nystagmus, more especially when the eyes are turned outward, especially toward the paretic muscle, areflexia or hyporeflexia of the cornea, tinnitus and diminished hearing on the same side, and cerebellar ataxia. He looks upon



this symptom-complex as typical, and says that whereas in the beginning he always made the diagnosis of cerebellar tumor on the affected side, he now knows that these are cases of acquired internal hydrocephalus or serous meningitis. The apparently focal signs of internal hydrocephalus are partly due to distal pressure. This would explain the paralytic signs on part of the cranial nerves at the base of the brain. Oppenheim says that a unilateral predominance of pressure in the labyrinth of one side may so affect the cochlearis and the nervus vestibularis as to cause staggering to one side, tinnitus, as well as the nystagmus, and the abnormal holding of the head.

As a rule, gross unilateral symptoms on part of the extremities are absent in acquired hydrocephalus, but they may be present, as we know from reported cases, prominent among which is the case of unilateral hydrocephalus reported by Spiller.<sup>62</sup> These, however, are the exceptions, and when they do occur they are not progressive or permanent (Oppenheim). The focal signs may be also explained by the fact that serous meningitis may be complicated by a mild localized encephalitis; or, what may also happen, the encephalitis may be the cause of the serous meningitis. Monoparesis, hemiparesis and hemianopsia are rare; still they have been observed (Annuske, Quinke and Kupferberg; for literature see Hoppe<sup>63</sup>).

Moreover, we may have attacks of convulsions, with periods of somnolence and coma, lasting perhaps a few days and then disappearing, perhaps not to return in months. The writer has seen this in a case of hydrocephalus which was associated with a brain tumor, and in which these attacks occurred six or eight times in a period of two or three years. Remissions are more common in brain tumor. Herzfeld calls attention to these attacks coming on with almost apoplectic suddenness after long periods of comparative well-being. Oppenheim attributes these attacks to a sudden increase of intraventricular pressure, or to a sudden compression of the medulla or vasomotor centers caused by a change in the position of the head.

We see, therefore, that there is a marked similarity not only between acquired hydrocephalus and cerebellar tumors, but also tumors of the brain in general. As a rule, time clears up the diagnosis, and even during life we can say with considerable certainty whether we have a case of tumor or hydrocephalus. If the patient dies, the condition, as a rule, becomes certain. But what of those cases in which the autopsy is entirely negative, or in which the patients recover and remain well? Nonne concludes that in the eight cases of brain-tumor complex with recovery which he reports in his article, there could not have been an acquired internal hydrocephalus or meningitis serosa, because of the absence of the etiological factors of the latter condition, namely: alcoholism, physical or psychical shock, insolation and infection.

It is possible, however, to have acquired hydrocephalus without any cause known or discoverable during life. We are inclined to think that at least some of these cases are due to acquired hydrocephalus taking its origin from some cause unknown during life, which is either favor-

ably affected by the treatment or disappears spontaneously, the exudation being resorbed.

Let us consider briefly the *etiology* of acquired internal hydrocephalus in regard to its pathology.

Spiller reports a case occurring in the service of Dr. Mills, in which during life the diagnosis of cerebellar tumor was made. The autopsy, however, revealed an internal hydrocephalus caused by closure of the aqueduct of Sylvius by proliferation of the neuroglia. Byrom Bramwell reports a similar case caused by a closure of the foramen of Magendie. J. Parkes Weber reports a case of acquired hydrocephalus with marked ependymitis of the fourth ventricles. He draws an analogy between acquired hydrocephalus and serous pleurisy and peritonitis. In both of these conditions we may have a large serous effusion caused by a small local area of inflammation; and he asks whether a large acquired hydrocephalus may not be caused in the same way. This conclusion would seem to be borne out by an autopsy which the writer recently made on a young boy, in which a marked hydrocephalus complicated a case of brain tumor. The tumor, an endothelioma, grew in the thalamus and extended into the white matter. Covering the serous surface of the lateral ventricle just over the tumor was a small area of tough fibrous exudate, about the size of a silver half dollar, which could be peeled off. In this case the symptoms were typical for acquired internal hydrocephalus, and antedated for years the focal signs of the brain tumor. It is not improbable to conclude that this hydrocephalus may have had its origin from this small area of inflammation which was found located over the tumor in the lateral ventricle.

We also know that autopsies do not always show a closure of the various foramina in internal hydrocephalus.

From the reports of well-examined cases we know that acquired hydrocephalus may occur from an inflammation of the tela choroidea, the choroid plexus (from pressure upon the vena Galeni), or a localized inflammation around the opening of the fourth ventricle. Any of these conditions might terminate in recovery. Anton says that a frequent cause of chronic acquired internal hydrocephalus is a localized meningitis at the base of the brain. Quinke and Bonninghaus say that this meningitis spreads to the tela choroidea and the choroid plexus, and in this way causes internal hydrocephalus. Any localized swelling or inflammation around the foramen of Magendie, or along the course of the canal of Sylvius, may lead to a closure of the passages, and thus cause an internal hydrocephalus. These various localized inflammations may yield to treatment, or heal spontaneously. The passages may reopen, the accumulated fluid become resorbed, and the brain may return to a normal condition.

Anton, Quinke, Gowers and Oppenheim are authorities for the fact that we may have recovery in typical cases of internal hydrocephalus acquisitus. The symptom-complex at times seen in myxedema of adults is probably due to a temporary meningitis serosa or internal hydrocephalus. Thus the author had a patient who has had myxedema for many years.

She was intelligent and highly educated. For years she has had attacks which begin with violent headache, vertigo, irritability, mental and emotional depression, marked staggering gait, delirium, mental confusion, and finally, after some days, inability to walk, terminating in great somnolence, apathy and apparent dementia. These attacks usually lasted from three to five days to as many weeks, and then terminated rather quickly when the thyroid extract was pushed. She had from one to four attacks a year for the last five or six years of her life, and they were looked upon as being due to an internal hydrocephalus, caused, perhaps, by the same toxin which causes the general myxedema. The author, therefore, feels that a large percentage of the cases of so-called brain tumor ending in recovery are really subacute cases of internal hydrocephalus which terminate in resolution. Included among these are those cases in which death has occurred, and in which the autopsy has been negative.

Have we any means of making the positive *differential diagnosis* between brain tumor and acquired hydrocephalus in these doubtful cases? It is needless to say to-day that the Quinke puncture, or the specific gravity of the fluid will not clear up the differential diagnosis. The factor of time itself will only enable us to say, in the recovered cases or in cases with a negative autopsy, that we did not have a tumor, but may have had an internal hydrocephalus.

(b) *Polioencephalitis Hemorrhagica*.—Polioencephalitis hemorrhagica usually is acute in its onset and rapid in its course. It does not ordinarily cause a symptom-complex resembling brain tumor. But the reported case of Schultze shows us how a polioencephalitis superior may simulate a tumor of the corpora quadrigemina, especially if it is complicated with an ependymitis with a secondary internal hydrocephalus. Schultze's case had, in addition to the focal symptoms, somnolence and optic neuritis. Oppenheim reports a similar case with recovery; he states also that he has had a number of such cases, one in which he had even advised an operation, and in which recovery occurred. He concludes that there was present either a non-purulent hemorrhagic encephalitis or some hitherto unknown pathological process capable of complete recovery.

Cases of completely cured polioencephalitis, with perhaps some slight defect, do undoubtedly occur. We have thus another condition which may cause all the signs and symptoms of a brain tumor and terminate in recovery. In these cases, according to Oppenheim, the localized encephalitis is in or near the cortex, which explains the occurrence of jacksonian epilepsy, monoplegia, aphasia, etc.

In this connection the author wishes to refer also to *meningitis tuberculeuse en plaque*, which Oppenheim looks upon as the cause of brain tumor symptom-complex occurring in a number of children who recovered. He (Oppenheim) looks upon the localized tuberculous meningitis as a curable affection (*see* chapter on Encephalitis). Therefore, as far as encephalomeningitis is concerned, we cannot always be absolutely sure

of the diagnosis because we cannot rule out, with certainty, either localized tuberculous or localized syphilitic meningitis.

(c) *Chlorosis*.—We know from the recorded cases of Crawford-Thompson, Burton-Fanny, Jollye, Gowers, that chlorosis may produce a symptom-complex which may temporarily simulate brain tumor. We have in these cases pronounced headache, vomiting, vertigo, together with optic neuritis. Oppenheim reports a case of especial interest, in which the anemia was a complication of carcinoma of the breast, and the headache, vomiting, vertigo, and optic neuritis simulated a metastatic carcinoma of the brain. The importance of recognizing the fact that anemia may produce a brain tumor symptom-complex should render us more careful about vetoing the amputation of a breast which otherwise might not only prolong the life of the patient, but even end in recovery.

(d) *Chronic Cerebritis*.—The consideration of pseudo-tumors of the brain with negative autopsy cannot be complete without taking into consideration the subject of chronic cerebritis or cerebral hypertrophy. This condition is exceedingly rare, and occurs most frequently in children, but may occur in adults. In adults where the cranium cannot expand we may have all the signs of intracranial pressure with irritation, resembling those of brain tumor. The cases are acute in their course, but may be subacute. The symptoms, according to Eulenburg, resemble very much those of acute hydrocephalus, violent headache, vomiting, slowness of the pulse, general convulsions, perhaps optic neuritis.

Let us see Rokitsansky's description of this condition: If we split open the dura mater we perceive immediately that there is a swelling of the brain, so much so that there is great difficulty in putting back the calvarium. The various membranes are remarkably thin, the dura mater is tender, pale red in appearance, the pia mater is very close on the one side to the dura, on the other to the cortex. They are abnormally dry and their vessels small, flat and usually free from blood; the brain hemispheres appear at first sight unusually large, the convolutions are pressed close together and flattened to such an extent that the sulci are hard to recognize. The white substance of the brain which has increased in volume is pale, anemic, which differentiates this condition from hyperemic turgescence. Rokitsansky looks upon the increase in size as due to an increase in the neuroglia. Anton holds that we may have also a parenchymatous hypertrophy of the brain. Rokitsansky and Eulenburg look upon the condition as due to a general increase of the neuroglia.

Eulenburg says that the fatal termination is usually due to a congestive hyperemia.

The literature on this subject is exceedingly small, but if such a case should occur and we were on the lookout for a tumor—especially if the brain were presented to us after the removal from the calvarium—the condition might easily be overlooked, and the autopsy considered negative.

Anton asserts that there may be a partial cerebral hypertrophy, which if it did occur might produce even a more decided brain tumor

symptom-complex. He gives, however, no data to substantiate this assertion.

(e) *Brain Tumors with Retrograde Changes or Arrested Development.*—In the cases of recovery from brain tumor we must bear in mind that the patient may really have had a brain tumor, and that the latter disappeared; or that the brain may have become accustomed to its presence after it had ceased to grow. Some of these cases, however, are cases of brain tumor with unusually long remissions of the symptoms, and not cases of real recovery; those like Osler's case finally end fatally. Oppenheim, Gowers, Bernhardt and Russell have reported similar cases. Psammomata, lipomata, cholesteatomata may attain a certain size and then cease to grow. Cysticerci and echinococci may die and shrink. The observations confirmed by autopsy are exceedingly rare. Nonne was able to find but four cases, those of Bruns, Oppenheim and Simeon.

Aneurysms may cease to grow or become obliterated by the formation of a clot and the brain accommodates itself to the pressure (Oppenheim, Hutchinson, Hodgson and Humble). Solitary tubercles may undergo caseation, calcification and then become encapsulated, causing no further damage (Wernicke, Starr, Knapp, Gowers, Babinski and Sahlberg). These observations are confirmed by the pathological observations of Simeon, who reports an autopsy in which a calcified tubercle was found which must have been in the brain for thirty years. Kirschberger's cases shows how a tubercle may show all the signs of a brain tumor for a year and a half and the patient recover and remain well for six and one-half years. The autopsy in this case showed that the tubercle had become calcified. Gummata may become absorbed and disappear.

Long remissions and even permanent disappearance of symptoms may occur in brain tumor, as numerous cases on record show. These cases, however, would hardly come under the head of pseudo-tumors with a complete disappearance of symptoms; because they had been regarded during life as cases of epilepsy of many years' duration, and after death, partly or completely ossified tumors had been found as the cause of the epilepsy.

That a pathological mass may be present in the cortex of the brain for 40 years and cause no interference with the ordinary daily life of an individual the following case will show (*see* Fig. 5):

Lately an individual, 60 years of age, died in the author's service at the Cincinnati Hospital from acute meningitis. He stated that at the age of 21 his left arm became paralyzed, but that it soon recovered. He had lived the life of a farmer and teamster for the past 40 years. With the exception of some weakness of the left arm and a constant headache he had always been well.

The autopsy revealed a mass, hard, indurated, cartilaginous, about the size and shape of a peanut, situated in the cortex at the posterior end of the first frontal convolution of the right side, pressing upon the ascending frontal convolution. This mass was partly cortical and partly subcortical, was not firmly adherent, and was surrounded by recent soft-

ening: On being split open, it was found to have a very hard stony calcareous center and a hard cartilaginous covering.

The practical conclusion of the consideration of this subject is: in the first place, we should not be too pessimistic in our prognosis of brain tumors, especially in cerebellar cases, until a considerable period of time has elapsed; and in the second place, we should not be too hasty in the recommendation of surgical interference both in children and in adults, until therapeutic measures have been given a complete test.

**COURSE AND DURATION.**—This subject, in a measure at least, is covered by the discussion of the general focal signs and symptoms, as well as by the pathology of the various forms of tumors. The course is always gradual, to be measured by months and years, rather than by weeks and days. Weeks, months, even years may elapse between the initial manifestations and the complete clinical picture. In the vast majority of brain tumors the course is a chronic one. The average duration, according to Oppenheim, is from two to four years, although they may last ten years or more. Exacerbations and remissions may occur. The growths may be quiescent for a period of weeks and months, during which time there may be few or no symptoms and signs. In the early stages the patient may have weeks at a time during which he is in apparently normal health. Other cases may go through stormy periods which are caused by intervening attacks of hydrocephalus. Some growths, like tubercles and gummata, may undergo retrograde changes and be quiescent for years.

On the whole, however, brain tumors are gradually progressive, and sooner or later present a complete clinical picture.

**Diagnosis.**—**DIFFERENTIAL DIAGNOSIS.**—The diagnosis of tumor of the brain is based upon two factors: one is the progressive loss of function of some part of the brain; the second is the fact that the tumor as it grows gradually adds to the volume of the cranial contents, and therefore increases the intracranial pressure. Both of these factors are very gradual in their development; both gradually cause symptom after symptom, and sign after sign, until in the course of weeks, months or years, the full-blown clinical symptom-complex, embracing both the general and focal symptoms, is developed. If we are careful to search into the clinical history of the case, and can trace the gradual progress of the disease and the adding of one clinical sign after another to those already in existence, we can usually make the differential diagnosis. The author has never resorted to using the puncture as a means of diagnosis and can see no reason for its use. Brain puncture, as introduced by Neisser and Pollak, is neither good surgery nor scientific diagnosis. It is working in the dark, and is accompanied by danger of hemorrhage. All the general signs must be indicative of increased intracranial pressure, all the focal signs must point to the fact that they have their origin from the destruction of a single area in the brain. Of course there may be in the exceptional case no general symptoms; or there may be, in addition to the local focal symptoms, distal signs, as, for instance, on part

of the sixth nerve; but the above rules should always be our guide, and we should keep in mind and give proper value to the exceptions.

*Cerebrospinal Syphilitic Meningitis.*—This disease, which is usually basilar, and affects the interpeduncular spaces and the area around the pons and medulla, offers one of the most frequent subjects for differential diagnosis. In this disease there will usually be a history of a more acute and rapid onset, a matter of days and weeks instead of weeks or months. The headache is more apt to be continuous and violent, with a tendency to rigidity of the neck muscles. Its clinical ensemble rarely points to a single location of the exudate, but it is usually cerebrospinal, with evidence of transverse, complete or incomplete involvement of the cord with a train of bilateral spastic symptoms of arms and legs with a disarrangement of the genito-urinary reflexes.

The pupillary changes are also typical, the pupils are usually unequal in size and paralytic, losing their reflexes both to light, accommodation and convergence, or we may have the pupils sluggish on one side and no reaction on the other. The papillæ are not always involved, and when they are, usually show a syphilitic exudate in and about the papillæ, rather than a papilledema. The field of vision is characterized by great irregularity, due to an irregular infiltration of optic chiasm, and optic nerves. The fields may show a zigzag rather than a concentric narrowing of the visual fields, or the field show a loss of irregular sectors when the two fields are compared. The external eye-muscles show a paralysis of the third nerve, usually on one eye, perhaps more marked on one side than on the other. There is apt to be a more or less irregular involvement of the other cranial nerves. Not infrequently we have either a hemiparesis setting in rather suddenly, or we may have an acute bulbar palsy following the initial signs and symptoms. Then, too, the mental symptoms are more rapid in their development, mental apathy and sluggishness often alternating with attacks, transitory delirium and mania. The *ensemble* of symptoms points to a multiple origin from the membranes of brain and cord. The laboratory tests are usually very positive in acute cerebrospinal syphilitic meningitis. There is an increased cell count, a positive Wassermann and the gold curve in the luetic zone. In brain tumor, Oppenheim very early called our attention to the fact that we might have a positive Wassermann reaction in glioma of the brain; and there is no reason why a brain tumor should not develop in a patient who has syphilis, but this is rather the exception. A brain tumor will not show an increased cell count nor a gold curve in the luetic zone. It is, however, not unusual to have a negative Wassermann reaction in a case clinically positively luetic.

*Paresis.*—As we have seen in case illustrated by Fig. 8, a tumor of the frontal lobes may run a clinical course similar to paresis. Within the past year a man was brought into the Cincinnati General Hospital with the diagnosis of paresis, because of the fact that he had periodic attack of general convulsions, mental hebetude and difficulty of speech, which later on was properly diagnosed as a subcortical tumor of the left parietal lobe in the region of the gyrus angularis.

The mental symptoms of paresis are characterized by a progressive dementia process rather than by mental hebetude. The speech disturbance is syllable stumbling with marked deterioration of memory. The focal signs are sudden in onset rather than progressive. In the early stages there is no motor aphasia. There are no signs of increased intracranial pressure. Again the cerebrospinal fluid will show an increased cell count, a positive Wassermann and the gold curve in the parietic zone.

When pupillary changes are present in paresis, which is often the case, we have an Argyll Robertson or a paralytic pupil, both of which are usually absent in brain tumor cases, except when they cause lesions in the optic tract. Optic neuritis is so rare in paresis as to deserve only passing mention.

*Multiple Sclerosis.*—The headache of multiple sclerosis is at times very intense, and we may have optic neuritis. But these general signs, which may remind us of the symptoms produced by increased intracranial pressure are usually absent in multiple sclerosis. Moreover, we have even early in the disease signs and symptoms pointing to multiple lesion of the brain, and especially of the spinal cord; nystagmus, scanning speech and intention tremor, when present, constitute a triad of symptoms seen only in multiple sclerosis. Nystagmus is often seen as a cerebellar or pontine sign, but intention tremor is not; scanning speech is essentially different from the cerebellar speech occasionally seen in tumor of the lobes of the cerebellum.

*Abscess of Brain.*—The differential diagnosis offers great difficulty between latent abscess in the quiescent stage and brain tumor. Latent abscesses rarely, if ever, present the signs of increased intracranial pressure. On the contrary, the periodic headaches in latent abscesses are caused by periodic flooding of the system with toxins, and are usually associated with general malaise, a slight rise of temperature and increased heart action. The blood may show changes, an increased leukocyte count would speak for brain abscess. So would also an increased cell count in the cerebrospinal fluid. There is more apt to be a state of general ill-health and progressive emaciation in brain abscess than in brain tumor. Brain abscesses can be differentiated from brain tumor when we have a distinct history of some sinus disease, middle-ear suppuration, or mastoid affection. Moreover, the focal manifestations are less distinct in brain abscess than in brain tumor, because of the infiltrating character of the suppurative process. The differential diagnosis in doubtful cases is very difficult. But the question is rather an academic one, because, if an abscess can be localized, it calls for the same treatment as a tumor—namely, radical surgical operation.

*Internal Hydrocephalus.*—The general symptoms of internal hydrocephalus and those of brain tumor may be identical, but the former rarely causes any focal symptoms, although Spiller<sup>22</sup> has placed a case of unilateral dilatation of a ventricle on record, with contralateral spastic hemiplegic signs. Here the diagnosis would be very difficult.



In the ordinary form, internal hydrocephalus presents bilateral spastic signs affecting in a very gradual manner both arms and both legs.

*Hysteria.*—While hysteria can simulate signs of brain tumor, it can never produce the objective manifestations, such as choked disk, and the signs of an upper motor neuron paralysis. We must remember, however, that hysteria frequently complicates brain tumor. Careful observation in these cases will enable us to separate the functional from the organic signs, and in this way arrive at a proper diagnosis. Hysteria will never be able to reproduce a real ankle clonus or a reversal of the plantar reflex. Babinski has also called our attention to various other signs by means of which an organic hemiplegia can be differentiated from a functional. The first is the platysma myoides sign. In organic cases the action of the platysma is absent on the paralyzed side; in functional hemiplegia it is present. In organic hemiplegia, when the individual attempts to arise from a lying-down position to a sitting position, the heel is raised from the bed, in hysterical paralysis the heel is pressed down into the bed. In a word, hysterical stigmata, whether motor or sensory, do not conform to the physiological laws governing the functions of the various centers and tracts of the brain, cerebellum or brain stem.

*Aneurysm.*—If for no other reason than a surgical one, it is very important to rule out aneurysms. Aneurysms may occur anywhere in the cerebral circulation, but are found oftenest in the middle cerebral and basilar arteries. We should always, when in doubt, first resort to the Wassermann test, because of the well-known relation of syphilis to the development of aneurysms. In the second place, we can at times distinguish a bruit over the probable seat of the aneurysm. Cushing maintains that a bruit is rare in real aneurysm and is more characteristic of the arteriovenous variety. We must also remember that a tumor may press upon a vessel in such a manner as to cause a murmur. Aneurysms, however, rarely give rise to symptoms during life, and the diagnosis is not often made. Beadles<sup>16</sup> analyzes 507 cases, in only 37 per cent. of which symptoms were manifested during life.

In early adult life syphilis is usually the cause of aneurysm, and in later life arteriosclerosis.

*Nephritis.*—Nephritis in its later stages, namely, during the uremic phases, may cause both general and focal symptoms, which may cause us to suspect a brain tumor. Moreover, an individual may have both chronic nephritis and a brain tumor; the symptoms produced by the brain tumor may be completely masked by those of nephritis in the late stages, and the tumor found only on autopsy.

Uremia may cause focal brain lesions (Hoppe<sup>63</sup>), both hemiplegia, aphasia, localized convulsions, etc., but these are always of a passing character and disappear with the passing of the uremic intoxication. The general nervous symptoms, viz., headache, vomiting, vertigo and optic neuritis, resemble closely those of brain tumor and according to Cushing are caused by increased intracranial pressure. The presence of albumin and casts in the urine and the high diastolic and systolic blood-pressure,

especially during the presence of the nervous manifestations, together with the fleeting character of the focal symptoms when present, should enable us to diagnose chronic nephritis, and rule out brain tumor. (For serous meningitis and pseudo-tumor complex *see* paragraph on Pseudo-tumor.)

**THE X-RAY AS AN AID IN DIAGNOSIS.**—Spiller<sup>84</sup> showed by autopsy that acute hydrocephalus or serous meningitis caused deep groovings of the interior of the calvarium, produced by the pressure of the convolutions, even in the absence of enlargement of the head.

Bertolotti,<sup>85</sup> in a case of acute hydrocephalus ending fatally in twenty days, showed that the inner surface of the calvarium presented grooves resembling finger-marks. Similar markings are not seen in brain tumor cases, and in secondary hydrocephalus, presumably because the pressure is more gradual.

Heuer and Dandy<sup>86</sup> have studied the roentgenography in the localization of brain tumors in 100 cases which have come to the service of Dr. Halsted. Of these cases, 96 were operated upon and in 68 cases the nature and localization of the lesion (not all were tumors) were accurately determined. From the viewpoint of *x-ray* diagnosis they divide tumors into three groups: (1) those which themselves cast a shadow in the *x-ray* plate; (2) those, which casting no shadow themselves, caused some deformation of the skull which could be recognized; (3) those which gave no evidence of their presence in the roentgenogram.

Few tumors come under the first heading. The majority come under the second group. Under the first come those tumors which have undergone a bony or calcareous degeneration, and also calcified walls of cysts, abscesses and aneurysms. This group is comparatively small. The bony or calcified mass is denser than the skull and therefore of lighter color than the surrounding bone. The calcified walls of cysts and abscesses and aneurysms throw ring shadows, complete or incomplete, which surround spherical masses. There may be, normally, calcareous degeneration of the pineal gland, as well as calcareous deposits in the choroid plexus and falx cerebri, and these must be taken into consideration when the plate is interpreted for evidence of tumor. Tumors which infiltrate sinuses can be demonstrated by the *x-ray*; because, displacing the air in the sinus, they will cast a shadow.

By far the greatest number of tumors (57) come under the second group: viz., those which cause recognizable deformities of the skull. These deformities are: (a) The enlargement of the skull as a whole, which enlargement is caused by (b) a separation of the sutures. They say that this separation was clearly apparent in 57 patients. Such separation, rare in cerebral, is common in tumors of the posterior fossa. (c) General convolution atrophy of the internal table of the skull. In this they confirm the findings of Spiller and of Bartolotti, who found these markings, made by pressure of the convolutions on the inner surface of the skull. These markings are most frequently seen in primary internal hydrocephalus. (d) Sellar destruction, especially of the posterior clinoid processes, found in tumors, not directly involving the sella;

viz., in cerebellar tumors, which they attribute to general increased intracranial pressure.

**Treatment.**—**MEDICAL.**—Medical treatment of brain tumors can be advocated under two heads: (a) curative; (b) symptomatic. On account of the fact that we cannot be absolutely certain in the early stages whether a tumor is present or of what nature the growth is, every case ought to be subjected to a six weeks' **antisyphilitic treatment**, even though the Wassermann reaction be negative. Grains 40 (2.6 grams) of **iodid of potassium** four times per day, and about fifteen **intramuscular injections** of some one of the **mercurial soluble salts** will be sufficient to cover this indication.

On account of the well-known fact that these cases wander from one physician to another, endless and needless repetition of this course on antisyphilitic treatment should be guarded against. If there is a suspicion of syphilis or a positive Wassermann, **arsphenamin** should be given intravenously. According to the author's experience, four to six doses will be sufficient. We are decidedly against the intraspinal use of **arsphenamin** in any form. The use of the **x-ray** and **radium** is indicated in brain tumors. Little reliance should be placed upon either of these before operative procedure. After a case has been operated upon, and the tumor only partly removed, radium treatment should be resorted to after the incision in the scalp has united. One or more applications directly over the seat of the tumor should be made. These applications should extend over a period of 6 to 8 hours.

There is no other curative medical treatment, and after 4 to 6 weeks recourse should be had to **surgery**, either radical or palliative. For the relief of headache, any of the coal-tar preparations may be used, **phenacetin**, **salipyrin**, **pyramidon**, either alone or in conjunction with **citrate of caffeine** or **monobromate of camphor**, or both. In cases in which surgical treatment is not indicated, **codein** or **morphin** must occasionally be given for the relief of pain. In lesions of the hypophysis, showing a preponderance of hypopituitary symptoms, the tablets of the **extract of the anterior lobe of the hypophysis** should be administered. **Spinal puncture** should not be resorted to for the relief of increased intracranial pressure because of the danger of jamming the medulla into the foramen magnum and, by compression, causing death.

**SURGICAL.**—Surgical operations are either radical, performed with a view of removing the tumor, or remedial, viz., decompression, when the tumor cannot be localized accurately. The old time exploratory operation with its attendant mortality (50 per cent. or more), due directly to the surgical interference, is no longer justifiable. We can say with Cushing that the brain is not a pie into which one can stick one's finger.

Great changes have taken place in our knowledge and experience, both with palliative and radical brain surgery. Twenty years ago radical brain surgery was limited to the motor area. Bergmann<sup>87</sup>—basing his opinion on an analysis of Hale White's 100 cases of brain tumors, found in the autopsy room of Guy's Hospital, Seydel's 50 cases, Allen Starr's<sup>88</sup> 600 cases compiled from all sources, and Oppenheim's 23 cases, all care-

fully observed *intra vitam* and after death—comes to the conclusion that at most but from 6 to 7 per cent. of all brain tumors can form the subject for surgical interference, and that to all intents and purposes brain surgery is limited to the psychomotor areas. There were no subtentorial operations. Removal of cerebellar tumors was not attempted. Palliative decompression was not practiced. No pituitary growth had been removed. The mortality, too, was rather high as a result of this surgical interference.

Von Hippel collected all the published operations on the brain, which he divided into two groups:

1. Those cases in which the brain tumor or cyst was accurately located and removed.

2. Those in which the localization was defective and the so-called exploratory operation was made.

The first group comprises 116 cases. In all of them the tumors were removed; and 60 per cent. of the cases were not benefited at all, or died as a result of the operation.

The condition, however, is entirely different in the so-called exploratory operations or in those cases in which, although the tumor was found, it was too large for removal. There were 157 of these cases and the operations were either useless or worse, for 47.7 per cent. died as the direct result of the operation.

The improvement in neurological diagnosis and the great advance in surgical technic have extended the field of radical surgery to every accessible part of the brain. Not only that, but the immediate, and in some instances, viz., the cerebellopontine angle, and the hypophysis, the remote results are infinitely better. In a recent publication Cushing reports 136 operations for brain tumor done in 18 months, among them 37 hypophyseal and 48 subtentorial, with only four deaths—a mortality of less than 3 per cent.

Brain surgery is always more or less of a hazard, because of errors in localization which will occur. Rather than allow the patient to die without a chance, and rather than do a palliative decompression, the great desire to remove a tumor leads to the temptation to operate over a given area, when all the localizing signs are not as sharply defined as they should be. This is a laudable, and perhaps a justifiable practice, but as Ransohoff<sup>89</sup> says, it leads to the result that in only 40 per cent. of the attempts is the tumor found. In the other 60 per cent. the operation then becomes more or less an exploratory operation, with the great mortality which attends these operations. When we speak of the mortality of surgical intervention we must always distinguish between the radical operation and the palliative decompression; the mortality of the former is still very high, and of the latter very low. The rule should be that unless the evidence is greatly on the side of accurate localization, the radical operation should not be attempted, but decompression should be resorted to. This opens up the all-important question as to when shall the operation be done.

The first and all-important rule is to operate early. This is especially

true in these cases in which accurate localization is possible. The smaller the tumor, the less damage is done to the brain, both locally and generally; the easier the tumor is to remove, and the less damage to the patient from surgical shock. But when there are no accurate localizing symptoms, and in less than 10 per cent. do these localizing signs occur early, the question of the time for an operation is all important. There is only one indication for deciding this question: the degree of papillo-edema, and the danger to the vision of the patient. Cerebellar tumors cause the most violent choked disks, and are notoriously the most difficult of diagnosis and localization.

Every case of papillo-edema caused by a brain tumor will lead to optic atrophy, unless the patient dies before this occurs or the intracranial pressure is relieved. Very frequently the operation is delayed until the atrophic changes have gone on to such a degree as to lead to total blindness, even after the tumor has been successfully removed. This is not always the case, but it is more apt to occur in subtentorial growths. It is advisable, therefore, while we are waiting for more evidence of accurate localization to develop, to have the visual field examined from time to time in order to determine the danger of loss of vision. De Schweinitz, on the other hand, advocates an early operation for all cases where papillo-edema is present, for he says that "good vision must not be allowed to stay the hand in operative interference, because what is good vision to-day may in a few days be poor vision, and already those processes may have started which, if unchecked, lead to the degenerations of the nerve, which ultimately end in blindness and atrophy."

If the tumor is of rapid growth, and a radical operation cannot be performed, even though the vision is failing, the author would advise against the decompressive operation, if relief could be obtained by coaltar preparations or morphin. The writer has seen what was apparently a metastatic tumor of the brain, with acutely developed choked disk, end in death in six weeks; another primary growth of the parietal lobe in which a radical operation was refused because no positive assurance of a cure could be given, end in death six weeks after the papillo-edema was developed. It would be folly in such rapidly growing tumors to advise palliative operation. The operation in all probability would not relieve the intracranial pressure and the brain hernia would add to the discomfort of the patient and hasten his death. The rule which the author would advocate, therefore, for papillo-edema is that, in the first place, we can safely wait until there is some objective disturbance of sight, as would be indicated by carefully watching the field of vision for white as well as for colors. This rule would give us time to determine whether or not the signs and symptoms will eventually indicate the possibility of a radical operation, with a chance of permanently curing the individual, rather than giving him merely temporary relief, although we must not forget that a secondary operation may be resorted to later, if the chance, or a radical operation, should offer itself. If we consider, according to the tables of Starr, Ferrier, Oppenheim, Walton, Paul and Tooth, that a radical operation is possible only in 10 per cent. of cases,

the above rule is a good one. We must, however, not be misled by the belief that the operation always affords relief, or that vision is always saved. Oppenheim, while advocating palliative trephining, if the disturbance of vision makes great progress, and while admitting that he has had numerous cases in which the headache, papillo-edema and general symptoms of compression were relieved for a long time, dissents from the radical views of Spiller, Frazier,<sup>90</sup> Säger, Paton, Cushing and others. He says that in part of his cases, aside from the diminution of the headache, no relief or improvement followed the operation, and in some cases the fatal termination was greatly hastened. In a few cases, too, the optic atrophy continues even after the palliative operation, and the patient becomes totally blind even though the papillo-edema has disappeared.

Having decided that a decompressive operation should be performed, no delay should be tolerated because of the reputed therapeutic value of iodid of potassium. Every day of procrastination means an increased liability that the patient might be unable to survive the shock of operation. This is especially true of subtentorial growths, whose pressure upon the medulla may at any moment produce such grave involvement of circulation and respiration as to make a suboccipital decompression operation inadvisable, on account of the probability of death occurring during the operation.

Cushing's views as to decompression, and where the operation should be performed, have rapidly gained ground, and with good reason. When a radical operation seems impossible and the tumor does not seem to be removable, Cushing advocates subtemporal decompression on the right side, except in a case of a growth so placed as to produce internal hydrocephalus. He maintains that it is undesirable to decompress over the presumed seat of a tumor, because the cerebral hernia leads to a dislocation of the parts and on account of the attending danger of hemorrhage into and around a vascular growth. In other words, it is a question of whether or not the old exploratory operation, with its high rate of mortality, shall be displaced by the Cushing operation. This operation is not without its opponents.

Oppenheim says that in the few operations which he had advocated according to the Cushing method he has seen little relief, but rather a more rapid exitus; although he has seen much benefit from palliative operations which were of an exploratory character when the tumor was not found. This would in a measure come near to the views expressed by Horsley, who was a strong opponent of the Cushing method. It may be apropos here to give Horsley's views on this subject, since all the neurological world is so very much taken up with and is advocating the Cushing operation. Horsley looked upon the subtemporal region as one of the dangerous locations of the brain. He says that if you draw a line laterally from the frontal eminence to the occipital protuberance, more shock results from operations below that line than above that line; also that the shock increases as we proceed from the frontal to the cerebellar pole of the encephalon; the danger is greatest in operations below

the tentorium on account of the presence of the vital centers in the medulla.

Horsley's statistics show that death from primary shock occurs once in twelve cases in operations in the temporal region, and once in ten cases in the cerebellar region. He does not mention, however, whether the above mortality from shock occurs in the simple decompressive operations, or in exploratory operations. Horsley's objection to subtemporal decompression is that it does not always relieve intracranial pressure. He advocates operating over the presumable location of the tumor, saying that if the tumor is not found, pressure is usually relieved.

There are two objections, in the author's opinion, to Horsley's views: In the first place, it re-advocates the exploratory operation, which has been condemned on account of the high rate of mortality. Oppenheim disagrees with Horsley's view, and takes sides with Cushing when he states that the above-named procedure (Horsley's) should only be followed when there is some probability that the tumor can be removed. The second objection, however, is equally valid, namely, the increased danger of a cerebral hernia, which is reduced to a minimum in the Cushing operation. Horsley's objection to the routine subtemporal decompression is that it does not always decompress. Of thirteen cases which died soon after the operation, seven died because the intracranial pressure was not relieved, for the reason that the opening was not made over the tumor. This argument loses some of its force because he does not give any autopsy reports nor does he state whether the tumors were cerebral or cerebellar, which makes a great difference. Sanger's views are partly in accord with Horsley's and Oppenheim's and partly with Cushing's. He says that we should invariably trephine over the fossa in which we suspect the tumor to be; in the absence of such information, under the right temporal muscle.

The rule at present is that subtemporal decompression on the right side should be done for tumors of the cerebral hemispheres, and that suboccipital decompression should be done for subtentorial growths. At least this would seem to be the general rule, although there is some doubt still present.

Spiller is an advocate of the suboccipital decompression, whenever a subtentorial growth is suspected. He maintains that the dangers from operative interference have been unduly exaggerated; that a faultless technic and a two-stage operation will greatly reduce the danger, and that the results of palliative operations on the cerebellum are more gratifying than similar operations on the cerebrum.

Cushing is not quite so positive: "It is generally supposed that in case of suspected subtentorial growth it is better to decompress through an opening in the suboccipital region. And this is certainly the preferable place, if one has been led to enter the skull at the occipital base with the reasonable hope of finding there a removable tumor; but otherwise I am not as certain as I would wish to be that the decompression is any more effectual than if accomplished by means of a defect placed elsewhere." He then reports a disastrous operation in the occipital re-

gion. The patient, on account of the great intracranial pressure, being practically decerebrated, and living in this condition for four months, "the natural conclusion was that the backward dislocation of the brain, which the suboccipital opening permitted, had caused a sudden and lasting compression of the brain-stem."

Sänger is also very optimistic, advocating suboccipital decompression for suspected subtentorial growths, ending his remarks with the statement that trephining over the cerebellum is not so dangerous as it was formerly thought to be.

The fact that we may find a localized serous meningitis instead of what was supposed to be a cerebellar tumor greatly strengthens the argument in favor of the suboccipital decompression. Krause reports that in fourteen operations for cysts of the cerebellum, thirteen recovered completely. On the other hand, in trying to decide the question for the individual case we must take into consideration the question of relative mortality of the two operations. The subtemporal operation is probably the less dangerous, although there are no statistics at hand to show it, but Frazier and Cushing state it to be so.

The mortality of operations over the cerebellum was very high; but, with improved technic, improved head rest and the two-stage operation, the mortality has been greatly reduced, as we have seen from Cushing's record given above. We quote Spiller again: "In Oppenheim's table of 1902, the mortality was 71 per cent.; in Duret's table, 1903, it was 42 per cent." Spiller's table for total number collected (116) shows a mortality of 42 per cent., and in cases reported from 1899 to 1905 death occurred in only 25 per cent. of cases.

The statement, therefore, that suboccipital operations are only a little more dangerous than the subtemporal, is, to say the least, not proven. That they give more relief is true. The author believes that the choice between the subtemporal and suboccipital operation will have to be decided on two points: first, the general condition of the patient, and second, whether or not the tumor case is complicated by an internal hydrocephalus. With regard to the first point, we must consider that the ideal case rarely occurs. Usually cerebellar tumors, and especially those of the cerebellopontine angle, are obscure. The general diagnosis of a brain tumor can be made, but often many months elapse before cerebellar signs are manifest; when the latter do occur they are often bulbar compression symptoms which threaten the life of the patient. The long illness has reduced the strength of the patient; pressure on the brain-stem threatens respiration and circulation; the patient is not in a condition to stand the shock of a severe operation, and is liable to die on the table. It would seem to the author that if pulse and respiration are fairly good, suboccipital decompression should be done; if they are not good, there should be preliminary subtemporal decompression. It is possible, however, that a suboccipital decompression, even under such adverse circumstances, might save the life of the patient. If the signs and symptoms all point to the fact that the case is complicated by an internal hydrocephalus and the signs and symptoms point to a sub-



tentorial growth, a suboccipital exploration should be attempted. It is admitted by all that a subtemporal decompression will not relieve the intracranial pressure, if caused by an internal hydrocephalus.

So much advance, especially through the work of Harvey Cushing, has been made in our knowledge of tumors of the hypophysis that a few words as to the surgical treatment are in place. This is all the more true since, with the increased knowledge of the hypophysis, the number of cases which are diagnosed has greatly increased in the past decade.

For a detailed statement of operative indications and methods, as well as technic, the reader is referred to Cushing's book.<sup>38</sup>

In 1914, Cushing<sup>91</sup> was able to give an analysis of his surgical results, based upon 148 cases of hypophysis disease, 101 of which were tumors. In discussing the surgical treatment, Cushing divides the cases into two groups:

- (1) Those in which the tumor is located above the sella;
- (2) Those in which the tumor is within the sella.

In the first group surgical measures are very unsatisfactory, except that relief may occasionally be given by sellar decompression.

In the second group he advocates very strongly the transsphenoidal route.

#### OPERATIONS FOR PITUITARY DISORDERS (Cushing)

	Cases	Opera- tions	Fatalities
Subtemporal decompression .....	33	37	2
Subtemporal explorations .....	8	8	0
Subfrontal explorations .....	5	6	1
Transsphenoidal decompressions .....	16	16	3
Transsphenoidal extirpations .....	52	58	4
	<hr/> 114	<hr/> 125	<hr/> 10

The operative mortality is 8 per cent. The case mortality 10.5 per cent.

Frazier<sup>92</sup> has adopted in his clinic the transfrontal approach, going through the side on which the frontal sinus is the smaller. He calls attention to the following advantages of the transfrontal approach: the facility of exposure; the opportunity of determining with some degree of accuracy the extent of the tumor; the avoidance of such contaminating influence as the secretion of the nasal mucosa, and the cosmetic results. In four cases there were no fatalities, and Elsberg advocated the frontal approach. Cushing is strongly in favor of the transsphenoidal route, as the above table clearly shows.

The following are the indications laid down by Cushing for the surgical measures in his book on Pituitary Diseases:

- (1) Sellar decompression: (a) for the relief of headaches; (b) for

the purpose of encouraging the extension of a glandular struma in the direction of the sphenoidal cells rather than into the cranial chamber.

(2) Partial removal of an hyperplastic gland in the active state of hyperpituitarism.

(3) Into the partial removal of a tumor or struma for the relief of neighborhood symptoms.

(4) Into subtemporal decompression for the palliation of pressure symptoms, when an intracranial extension has occurred.

(5) Into a subtemporal or sellar decompression or both, to permit of the more favorable and direct application of radium therapy.

(6) In the exposure of the brain or some other organ in the case of marked hypopituitarism for the purpose of implanting a viable organ.

An operation for relief of a cyst of the pineal gland was attempted by L. Pussep,<sup>93</sup> who entered through the occipital region and then made an incision through the tentorium cerebelli.

**Prognosis.**—It is unnecessary to repeat what has just been said about gummata and tubercles. Their calcification and quiescence occur only rarely.

Occasionally a tumor will burrow its way through the bony skull (autotrepation) and appear as a swelling under the scalp. The author has seen this once. Tumors on or near the surface can be successfully operated upon. Gliomata, being infiltrating, are less favorable than sarcomata, which can be completely removed. Much good can be accomplished and relief given and life prolonged by decompression, when radical operations are not possible. The prognosis of cerebellar tumors and tumors of the cerebellopontine angle is much better as a result of an improved technic than was the case a decade ago.

Cysts and adenomata of the hypophysis are now successfully operated upon. The prognosis of subcortical growths and tumors of the basal ganglia, as well as those of the corpora quadrigemina, pons and medulla, is bad. Those of the brain-stem and peduncles should not be operated upon at all. Tooth,<sup>94</sup> in a study of 500 cases, inquired into the life history of tumors, verified by postmortem and untouched by surgery. He speaks of the survival period of tumors from the appearance of the first symptoms to death. The average survival period of gliomata is 10.1 months and varies a little, according to the location, gliomata of the pons averaging 9.4 months. Endotheliomata are of longer duration, the survival period being about four years. Sarcomata survive 11.2 months; carcinomata, 10.1 months; tuberculomata, 17.4 months.

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## CHAPTER IX

### DISEASES OF SPECIAL NERVES

By CHARLES METCALFE BYRNES, M.D.

- The cervical nerves, p. 709:—Cervico-occipital neuralgia, p. 710; Indurative headache, p. 710; Phrenic nerve, p. 713.
- The brachial plexus, p. 714:—Anatomy, p. 714; Diseases of the brachial nerves, p. 716:—Paralysis of the brachial plexus, p. 716; Combined palsies of the upper extremity, p. 717; Lesions of the upper trunk—the Duchenne-Erb or upper arm type of palsy, p. 717; Lesions of the lower trunk—Klumpke or lower arm type of paralysis, p. 719; Obstetrical paralysis—Duchenne-Erb birth palsy, p. 719; Cervical rib, p. 721—Posterior thoracic nerve, p. 725; Suprascapular nerve, p. 727; Axillary or circumflex nerve, p. 728; Radial or musculospiral nerve, p. 729; Musculocutaneous nerve, p. 732; Median nerve, p. 732; Ulnar nerve, p. 734.
- The intercostal nerves, p. 737.
- The lumbar and sacral plexuses, p. 737:—Lumbar plexus, p. 737; Sacral plexus, p. 739:—External cutaneous nerve, p. 739:—Meralgia paresthetica, p. 739—Obturator nerve, p. 741; Femoral or anterior crural nerve, p. 741:—Neuritis of the femoral nerve, p. 742—Superior gluteal nerve, p. 742; Sciatic nerve, p. 743; Tibial or internal popliteal nerve, p. 744; Common peroneal or external popliteal nerve, p. 745; Plantar nerves, p. 746.
- The sciaticas, p. 746:—Definition, p. 746; Types of ischialgia, p. 747; Incidence, p. 747; Etiology, p. 747; Symptomatology, p. 749:—Special methods of examination, p. 750:—Lasègue's sign, p. 750; Kernig's sign, p. 751; Patrick's sign, p. 751; Sign of the great toe, p. 752; Sensory Achilles sign, p. 752—Laboratory examinations, p. 753—Diagnosis, p. 753; Complications, p. 754; Treatment, p. 754; Prognosis, p. 755; Pathology, p. 755.
- Multiple neuritis, p. 755:—Types of multiple neuritis, p. 756; Etiology, p. 757; Symptoms of multiple neuritis in general, p. 759:—Sensory symptoms, p. 760; Motor symptoms, p. 761; Cranial motor nerves, p. 761; Sphincter disorders, p. 762; Reflexes, p. 762; Trophic and vasomotor symptoms, p. 762; Mental disturbances, p. 763—Diagnosis, p. 763; Complications, p. 764; Treatment, p. 765; Prognosis, p. 766; Pathology, p. 766.
- Special forms of multiple neuritis, p. 767:—Alcoholic neuritis, p. 767; Arsenical neuritis, p. 768; Neuritis due to lead poisoning, p. 769; Diabetic neuritis, p. 769; Diphtheritic paralysis, p. 770; Recurrent polyneuritis, p. 771; Progressive interstitial hypertrophic neuritis, p. 771; Acute febrile polyneuritis and neuronitis, p. 772.
- Bibliography, p. 773.

### THE CERVICAL NERVES

After the union of its component roots, the typical spinal nerve divides into an anterior and a posterior primary division; and, in the

cervical region, the anterior divisions of eight spinal nerves unite to form two important plexuses. The first four nerves are contributed to the cervical plexus; and the fifth, sixth, seventh, and eighth, together with the larger part of the first thoracic nerve, join in the formation of the brachial plexus. This plexus also receives, very often, a communicating branch from the fourth cervical nerve. The posterior rami are, as a rule, of little clinical importance; and, with the exception of the first cervical nerve, which is entirely motor, they innervate, in general, the skin and deeper musculature on the posterior aspect of the neck. The second cervical nerve furnishes, however, a large cutaneous branch which has some clinical significance. Its posterior primary division pierces the cranial aponeurosis just below the superior curved line of the occiput, as the great occipital nerve, and is distributed to the skin of the occipital region as far forward as the vertex.

The cervical plexus, soon after its formation from the anterior primary divisions, separates into deep and superficial branches, which are distributed to some of the muscles of the neck anteriorly, and to the integument on the posterior surface of the ear and scalp and the anterolateral region of the neck as far as the clavicle. Thus, the small occipital, the great auricular, and the superficial cervical nerves are entirely sensory, and do not possess the clinical interest attached to the deep motor branches, from which originates the important phrenic nerve to the diaphragm.

Because of its protected position, the cervical plexus is only occasionally the seat of disease or injury. Its branches may, however, be implicated in lesions of the vertebræ, in tumors and glandular enlargements of the neck, and in certain forms of external violence; and the nerve roots are sometimes involved in syphilitic affections of the spinal cord and in syringomyelia. Nevertheless, certain types of headache, neuralgia, and other painful affections of the cervical nerves are not uncommon symptoms; and herpes of the neck and occiput, with or without an associated facial palsy, is occasionally observed.

**Cervico-occipital Neuralgia.**—Pain in the distribution of the auricular, the small occipital, and particularly the great occipital nerves is sometimes a distressing affection. The disorder is more common in women than in men, and in many instances, exhibits the features of a true neuritis, with numbness, tingling, and paresthesia; but actual loss of cutaneous sensation is uncommon. Usually, the pain is of a dull, aching, throbbing, or burning character, and often localized in the nape of the neck, the occiput, or mastoid region. Its intensity and duration are variable, although it rarely exhibits the paroxysmal character of a definite neuralgia. Generally, the continuous suffering for a period of days or weeks is followed by an equal interval of relief; and often there is tenderness upon firm pressure over the superficial exit of the affected nerve. In protracted cases, relief has been secured by injecting the nerve with alcohol, as it pierces the cranial aponeurosis; and Von Hofmeister describes a rebellious case of traumatic neuralgia of the third cervical nerve in which resection of the posterior spinal root was resorted to before relief was secured.

**Indurative Headache.**—Recognition of the disease is due largely to the studies of Henschen who, in 1881, described an interesting and probably not uncommon painful affection of the cervical nerves, known as nodular, indurative, or rheumatic headache. The disorder was later

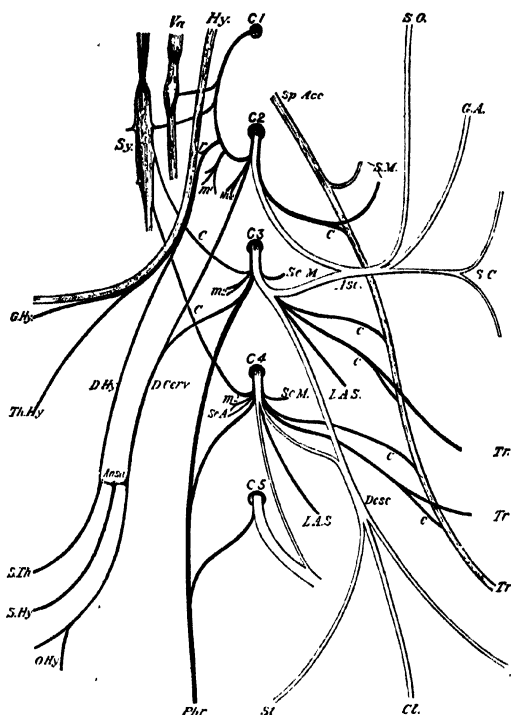


FIG. 1.—THE CERVICAL PLEXUS (After Cunningham).

**Superficial Division.****Ascending branches (Asc.).**

- S. O. Small occipital.
- G. A. Great auricular.
- S. C. Superficial cervical.

**Descending (supra-clavicular) branches (Desc.).—**

- Acr. Acromial.
- Cl. Clavicular.
- St. Sternal.

**Deep Division.****External branches.—**

- Communicating (C.) to spinal accessory nerve (Sp. Acc.).

**Muscular—**

- S. M. Sterno-mastoid.
- Tr. Trapezius.
- L. A. S. Levator anguli scapulæ.
- Sc. M. Scalenus medius.

**Internal Branches—****Communicating to**

- Hy. Hypoglossal.
- Va. Vagus.
- Sy. Sympathetic ganglion.
- D. Cerv. Descendens cervicis.

**Muscular**

- M1. Rectus capitis anticus minor, and lateralis.
- M2. Longus colli, and rectus capitis anticus major.
- Sc. A. Scalenus anticus.
- Phr. Phrenic nerve.
- G. Hy. Nerve to genio-hyoid.
- Th. Hy. Nerve to thyro-hyoid.
- D. Hy. Descendens hypoglossi.
- Ansa. Ansa hypoglossi.
- S. Th. Nerve to sterno-thyroid.
- S. Hy. Nerve to sterno-hyoid.
- O. Hy. Nerves to omo-hyoid.



recognized in Germany, in the writings of Noström, Rosenbach and others; and, more recently, the subject has been carefully reviewed in the instructive monograph by Siegmund Auerbach. Yawger, of Philadelphia, finds the affection not uncommon in America, and the author has met with several instances in which the symptoms appeared to be due to this variety of headache.

Women are said to be more frequently affected than men, although the condition is usually attributed to a chronic rheumatic disorder in which cold, exposure, and occupation are thought to be prominent **etiological factors**. The onset of the disease is insidious, and occurs most frequently within the third or fourth decade. Pain, not unlike that described in cervico-occipital neuralgia, is a constant feature and, very often, is of many years' duration. Nocturnal exacerbations are common, and atmospheric conditions appear to have some effect upon the intensity of the suffering. Usually, the symptoms are most pronounced in the cervical and occipital regions, but at times may involve the entire head, or radiate to the shoulder and arm. Neuralgic attacks of sharp pain may dart along the course of the nerve, and tenderness of the scalp or a sense of general discomfort about the head and neck is nearly always present; but the intermissions of complete relief, characteristic of most neuralgias, are not a feature of the disease.

The **diagnosis** rests upon the discovery of palpable nodular masses in the occipital and temporal fascia, within the substance of the posterior muscles of the neck, and particularly along the borders of the sternomastoid and trapezius. The nodules vary in size from a few millimeters to one or two centimeters; and, although of variable consistency, they may occasionally be rolled under the palpating finger like a small shot, or the larger ones may fade imperceptibly into the surrounding muscular tissue. The fibrous masses are usually intensely sensitive to pressure, and when firmly palpated, the characteristic neuralgic attack of referred pain is often reproduced. Occasionally, the lesions are demonstrable in the roentgenogram, and the author recalls an instance in which numerous perfectly round bodies, the size of grape seed, were clearly visible in the radiograph. The roentgenologist at once inquired if the patient had received a gun-shot wound of the neck. Histological examination of the nodules has usually revealed an indurative myositis with varying degrees of fibrosis and, in some instances, actual calcification.

Generally, the **prospect of recovery** is good, and massage is said to be the most effective remedy. In the beginning the **treatments** are often acutely painful, and may, for a time, aggravate the symptoms; so that it is advisable not to practice too vigorous or too prolonged massage. At first, **manual massage for five or ten minutes daily** is usually well borne, and as the patient becomes more tolerant of the treatments, more intensive manipulation may be practiced. By this means the nodules diminish in size, become less sensitive, and sometimes disappear entirely, with consequent alleviation and final relief of the headache. The author has, upon several occasions been able to confirm the therapeutic value of massage in these cases; but successful treatment depends upon the accuracy of the diagnosis and the persistent use of skillful massage. Differentiation of the myositic nodules from the glandular enlargement of a mild cervical adenitis requires, however, a certain degree of palpatory experience; and it is desirable, therefore, to make a practice of manual examination of the head and neck. Usually, the

larged lymph glands are less sensitive; they are not imbedded in the muscular substance, or attached to the cranial fascia; and forcible palpation does not reproduce the pain characteristic of indurative headache.

**The Phrenic Nerve (C. 3, 4, 5).**—Three cervical roots contribute to the formation of the phrenic nerve, but the larger part of its fibres is derived from the fourth cervical segment. The nerve trunk, composed of sensory, motor, and sympathetic fibres, is deeply situated in the neck, and descends into the thorax to become the principal motor nerve of the diaphragm. Sensory filaments are, however, distributed to the pleura, the pericardium and, through the sympathetic system, to the suprarenal capsule, the hepatic plexus, and the inferior vena cava. (Fig. 1.) Schroeder and Green have studied the formation of the phrenic nerve, and found that in 37 per cent. of one hundred dissections, it originated from the fourth and fifth cervical roots, while in 25 per cent. it was formed from the fourth root alone. Occasionally, filaments were contributed by the third, fourth and fifth roots, and less frequently from the third and fourth only. An accessory phrenic nerve arising from the fifth or, more rarely, the fifth and sixth cervical nerves, is sometimes present; and the diaphragmatic plexus also receives additional fibres from the last three intercostal nerves. Thus, while injury to the phrenic nerve ordinarily causes marked respiratory embarrassment, the accessory innervation of the diaphragm may, at times, prevent complete paralysis of the muscle.

Either local or systemic disease may be the cause of phrenic nerve paralysis. Congenital bilateral paralysis of the diaphragm has been noted, and Bernhardt refers to incomplete development of the muscle in an adult sixty years of age. Fracture, dislocation, and Pott's disease of the cervical vertebræ have resulted in paralysis of the nerve; and, occasionally, it has been injured from faulty position of the arm during ether narcosis, from the injection of novocain into the brachial plexus, and during surgical operations about the neck. Disease of the spinal cord, meninges, and vertebræ may implicate the phrenic nerve. Thus, paralysis of the nerve has been observed in syphilitic and tuberculous affections of the cord, in hematomyelia, spinal tumor, syringomyelia, progressive central muscular atrophy, and, according to Gerhardt, in tabes dorsalis. Diaphragmatic palsy has also resulted from pressure upon the nerve by aneurysm and other intrathoracic tumors, and from disease of the mediastinal lymph glands; and in pleurisy with effusion the diaphragmatic movements are sometimes obliterated.

Occasionally, the nerve has been involved in the toxic and infectious diseases, and phrenic paralysis in diphtheria, influenza, and alcoholic polyneuritis is usually of grave significance. Duchenne has noted paralysis of the nerve in chronic lead poisoning. A rheumatic or refrigeratory type of phrenic paralysis, analogous to that affecting the facial nerve, has been described, and the nerve is sometimes involved in acute infectious arthritis. A so-called functional or hysterical paralysis of the diaphragm is referred to by Bernhardt; and, in certain cases of shell-shock, Watson has recorded a peculiar type of diaphragmatic involvement, characterized by acceleration of the respiratory rate and a disturbance of the costo-abdominal rhythm. The symptoms are said to have disappeared during sleep.

**SYMPTOMATOLOGY.**—With the exception of pain, little is known of the sensory manifestations of disease of the phrenic nerve. A diaphrag-

matic neuralgia has, however, been described, and is usually attributed to an irritative lesion of the nerve or its terminal branches; but Schroeder and Green are of the opinion that hiccough, sneezing, and spasmodic coughing are not, as is commonly taught, evidence of phrenic irritation.

The paralytic and motor symptoms are better known and more easily recognized. One or both nerves may be involved; and in the unilateral affection the clinical symptoms may be so slight as to escape ordinary notice, or they may be entirely wanting. Dyspnea, cyanosis, increased respiratory rate, and disturbance of the costo-abdominal rhythm are common symptoms of the bilateral affection; but Cowan has observed complete phrenic paralysis in which the respiratory rate was not increased, and it is his opinion that this is not an essential feature. Because of the negative intrathoracic pressure, the respiratory movements are usually accompanied by widening of the costal arch and retraction of the epigastrium. Coughing and sneezing are often difficult or impossible, and voluntary protrusion of the abdomen is inhibited. The liver and spleen do not descend with inspiratory movements, and defecation is performed with difficulty. Occasionally, the absence of diaphragmatic excursions is demonstrable in the radiogram. Electrical excitability of the nerve is greatly diminished or lost; and Bernhardt has found it decreased in severe carbon monoxid and chloroform poisoning, although there was no actual paralysis of the diaphragm.

**DIAGNOSIS.**—In the unilateral affection the diagnosis is often difficult, and restriction or absence of diaphragmatic movement does not necessarily indicate disease of the phrenic nerve. Pleural and abdominal effusions may inhibit the action of the diaphragm, and fatty degeneration of the muscle in diphtheria may be mistaken for disease of the phrenic nerve.

**PROGNOSIS.**—When only one nerve is involved, the affection is said never to be fatal, and complete return of function may be expected unless there is some mechanical obstruction to the process of regeneration. The paralyzes of diphtheritic and, so-called, rheumatic origin, usually have a favorable outlook; but pulmonary infection and hypostatic congestion of the lungs necessarily add to the gravity of the situation, and the prognosis in the bilateral affection, especially when part of a multiple alcoholic neuritis, is particularly ominous. If, however, the alcoholic paralysis is not fatal in the acute stages, and there are no complications a more hopeful opinion may be entertained.

### THE BRACHIAL PLEXUS (C. 5, 6, 7, 8; T. 1)

**Anatomy.**—Ordinarily, the plexus is formed by the union of the anterior or ventral divisions of the fifth, sixth, seventh and eighth cervical, and first thoracic nerves. Often a communicating branch is received from the fourth cervical; and Kerr, in a study of 175 brachial plexuses, found it present in about 62 per cent. of the cases. He was unable, however, to make accurate observations upon the lower, or thoracic portion of the plexus; but it is generally accepted that a communicating branch usually exists between the first and second thoracic nerves, and that the second thoracic root also furnishes a more or less constant anastomosis through its intercostobrachial division. The relative size of these accessory communicating branches varies. Thus, when the fourth cervical contribution is unusually large, the first

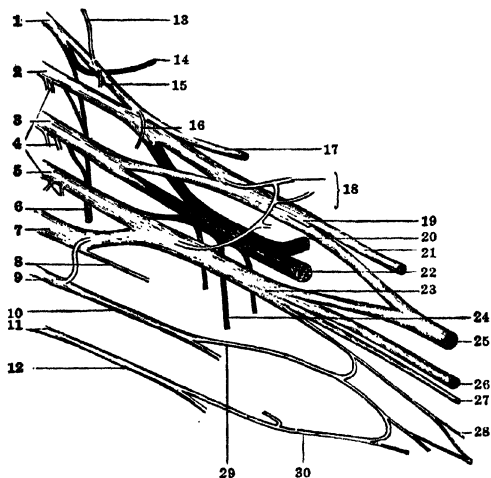


FIG. 2.—BRACHIAL PLEXUS (After Morris).

- |                                |   |
|--------------------------------|---|
| 1. Fifth cervical              | 17. Suprascapular                                 |
| 2. Sixth cervical              | 18. Anterior thoracic nerves                      |
| 3. Seventh cervical.           | 19. Lateral cord of plexus                        |
| 4. To scaleni and longus colli | 20. Axillary (circumflex)                         |
| 5. Eighth cervical             | 21. Musculo-cutaneous                             |
| 6. Long thoracic               | 22. Radial (musculo-spiral)                       |
| 7. First thoracic              | 23. Medial cord of plexus                         |
| 8. First intercostal           | 24. Thoraco-dorsal                                |
| 9. Second thoracic             | 25. Median  |
| 10. Second intercostal         | 26. Ulnar   |
| 11. Third thoracic             | 27. Medial antibrachial cutaneous                 |
| 12. Third intercostal          | 28. Medial brachial cutaneous (nerve of Wrisberg) |
| 13. From fourth cervical       | 29. Intercosto-brachial                           |
| 14. Dorsal scapular            | 30. Lateral cutaneous                             |
| 15. To phrenic                 |   |
| 16. Nerve to subclavius        |   |

thoracic component may be greatly reduced in size, or even wanting; and the plexus is then said to be prefixed or expanded. Occasionally, the first thoracic root is particularly well-developed, and there may be an abnormally large communicating branch from the second intercostal nerve. Under these conditions, the fourth cervical component may be absent, and the fifth cervical may be only partly concerned in the formation of this postfixed type of plexus. It cannot be stated with certainty, however, that the second thoracic nerve is, under these circumstances, always abnormally developed or directly joined to the first root; but it is generally recognized that at least five spinal nerves unite in a more or less constant fashion in the formation of the brachial plexus.

From the anastomoses of the five nerves are formed the trunks and cords of the brachial plexus. Thus, in the ordinary type of plexus, the fifth and sixth nerves unite to form the upper trunk, the seventh nerve remains alone as the middle trunk, and the eighth cervical and first thoracic nerves constitute the lower trunk. (Fig. 2.) These trunks then divide into anterior and posterior branches, which later unite to form the cords of the plexus. The anterior divisions of the upper and middle trunks join in the formation of the outer or lateral cord; the anterior branch of the lower trunk remains ununited as the inner or medial cord; and the posterior divisions of all three trunks unite to form the posterior cord. The posterior branch of the lower trunk contains, however, only a few fibres from the first thoracic nerve, and may originate entirely from the eighth cervical segment. From these three cords, so named because of their disposition about the axillary artery, are derived most of the nerves of the upper extremity. Some of the smaller motor nerves, and particularly those to the rhomboids, the serratus magnus, and the spinati arise at a higher level from the supraclavicular portion of the plexus.

**Diseases of the Brachial Nerves.**—Morbid conditions affecting the spinal nerves are not necessarily confined to local disease of the nerve trunk. This is particularly true of the brachial plexus, in which certain well-known diseases of the spinal cord are often associated with symptoms confined, at first, to one or more of the cervicothoracic segments. Thus, syringomyelia, progressive central muscular atrophy, and poliomyelitis may be the cause of motor or sensory disturbances in the upper extremity. Tumors of the lower cervical cord, syphilitic or tuberculous meningitis, disease of the cervical vertebræ, carotid aneurysm, cervical adenitis, and tumors of the neck may readily implicate the roots or trunks of the brachial plexus. Injury and disease of the shoulder joint, crutch pressure, and malposition of the arm during operations upon the breast are familiar causes of peripheral nerve lesions of the upper extremity. Brachial neuritis of toxic or infectious origin, and neuralgia of the plexus are not uncommon; and, with the exception of symptoms peculiar to the location of the lesion, do not differ from these affections situated elsewhere. Injury to the plexus during parturition, a frequent source of brachial paralysis, will be more fully treated in considering the obstetrical or birth palsies.

**PARALYSIS OF THE BRACHIAL PLEXUS.**—Complete paralysis of the brachial plexus is of unusual occurrence; and, even in the most extensive lesions the nerves to the rhomboids, the serratus mangus, the levator anguli scapulæ, and the subscapularis generally escape. Usually, the paralysis is the result of some form of external violence; and fracture, dislocation,

and gun-shot wounds of the upper extremity may cause widespread lesions. Krumholtz has observed almost total paralysis of the arm following an accident in which the patient was thrown from a racing-car, and in a second instance as the result of a fall from a scaffold. In traumatic paralysis the nerve cords or trunks appear to suffer most severely; and it is this circumstance which accounts for the escape of those nerves originating from the more proximal portion of the plexus. Neuritis of the plexus is sometimes the cause of extensive paralysis of the upper extremity.

As the result of a complete lesion, the entire extremity hangs motionless at the side; the muscles are toneless and flabby; and there is loss of cutaneous sensibility throughout the forearm and hand. Sensation is also lost on the outer aspect of the arm in its lower two-thirds; but on the inner surface of the arm and in a small area over the deltoid muscle, innervated respectively by the intercostobrachial nerve and the acromial branches of the cervical plexus, sensation is generally preserved. Pupillary changes, resulting from injury to the cervical sympathetic, are not uncommon; and, in severe cases, atrophy, the reaction of degeneration, and contracture make their appearance.

The prognosis depends upon the nature and extent of the lesion. With actual interruption of anatomical continuity complete recovery cannot reasonably be expected, but in the milder degrees of trauma, and in the neuritides the outlook is more favorable. Occasionally, there may be a prolonged residual palsy of the upper or lower arm type, or of certain groups of muscles, although the condition is not necessarily permanent. Reference has already been made to one of the author's patients who suffered for many months from complete paralysis of the brachial plexus. Partial recovery then ensued and, after remaining stationary over an extended period, terminated in complete restoration of function. Dereum has also recorded a similar experience. Nevertheless, in most instances, a guarded prognosis should be made.

**COMBINED PALSIES OF THE UPPER EXTREMITY.**—With the exception of the radial and ulnar nerves, which are sometimes severed or compressed in the lower part of the arm and at the elbow, lesions of the brachial plexus are rarely confined to a single nerve. Although the injury be inflicted distal to the formation of the trunks and cords of the plexus, it may very often be associated with multiple nerve involvement; but lesions of this type do not produce the symptoms of a combined palsy, in which the paralysis conforms to the radicular grouping of nerve fibres. Thus, in the typical lesion, one of the trunks or cords usually suffers, with resulting paralysis of a single nerve, such as the supra-scapular, which originates entirely from the upper trunk, and in addition, partial paralysis in the distribution of the several branches which receive a portion of their fibres from the injured trunk. Either the upper, the lower, or the middle trunk may be involved, although a lesion confined to the middle trunk is said not to have been observed. The cords of the plexus are less frequently injured, since they occupy a more protected position and, unlike the trunks, are not subjected to the same degree of tension in movements of the arm, or in lateral traction upon the head.

**LESIONS OF THE UPPER TRUNK—THE DUCHENNE-ERB OR UPPER ARM TYPE OF PALSY.**—Since the upper trunk is formed by the union of the fifth and sixth cervical roots, it is evident that implication of these fibres in disease of the spinal cord, meninges, or vertebræ will, in addition to

other features, be productive of symptoms analogous to those following a lesion of the trunk. The typical shoulder-arm paralysis is, however, ordinarily the result of injury or disease of the upper trunk alone. Thus, continued pressure in the supraclavicular region, a fall or a blow upon the shoulder, forcible abduction of the arm, and malposition of the arm during prolonged general anesthesia are important sources of injury. Although pressure alone may be sufficient to produce the paralysis, it is believed that in many instances there is actual rupture of some or most of the fibres of the trunk or roots. This is most likely to be true when the plexus has been subjected to sudden violent traction. To this type of paralysis belongs, also, one group of the obstetrical palsies; and reference has already been made to its occurrence as a residual feature in certain cases of complete paralysis of the brachial plexus. Occasionally, the bilateral affection is noted: and its occurrence has been recorded in neuritis, in arthritis, and, according to Lhermitte, in three instances following the administration of antitetanic serum.

The symptoms, then, of injury to the upper trunk are due to the interruption of fibres which contribute to the formation of the following nerves: the musculocutaneous, the suprascapular, the axillary, the radial, the anterior thoracic, the subscapular, and, rarely, a portion of the long thoracic and the nerve to the rhomboids. Ordinarily, the resulting paralysis is confined largely to the deltoid, the supraspinatus, the infraspinatus, the biceps, the brachialis anticus, and the brachioradialis. In the more extensive lesion, the rhomboideus, the subscapularis, the pectoralis major, the serratus magnus, the latissimus dorsi, and the extensors of the wrist may be affected. Fibres from the sixth cervical root are contributed through the median nerve to the pronator radii teres, the flexor carpi radialis, and the thenar muscles; but paralysis of these muscles is rarely observed in the milder degrees of injury. Actual loss of cutaneous sensation is uncommon, but pain, paresthesia, and hypesthesia have been noted along the radial border of the arm; and Oppenheim has described trophic disorders as of rare occurrence.

The clinical result of this extensive motor disturbance is a flaccid type of paralysis affecting principally the shoulder and upper arm. The extremity hangs close to the trunk with the forearm pronated. The arm cannot be abducted; flexion at the elbow and supination are greatly restricted, or impossible; and occasionally, external rotation of the arm and extension of the wrist are imperfectly performed. The paralyzed muscles soon exhibit the reaction of degeneration, and after a time become intensely atrophic with loss of all electrical irritability. Erb has shown that the upper trunk may be electrically stimulated at a point 3 cm. above the clavicle, and 3 cm. lateral to the posterior border of the sternomastoid muscle. In the normal individual stimulation of Erb's point is followed by contraction of all the muscles innervated by the fibres of the upper trunk; so that electrical examination at this point is often a valuable diagnostic and prognostic procedure. Restoration of function depends largely upon the nature of the injury. In the pressure palsies and inflammatory lesions of the trunk, the prognosis for recovery is generally hopeful, although the symptoms may persist for many months. If, however, the nerve fibres have been actually torn, or otherwise severely damaged, it is more than likely that some evidence of the disease will persist.

**LESIONS OF THE LOWER TRUNK—KLUMPKE OR LOWER ARM TYPE OF PARALYSIS.**—The component fibres of this trunk, formed by the eighth cervical and first thoracic roots may, like those of the upper trunk, be involved in disease of the spinal cord, meninges, or vertebræ; and paralyses of this type have been described in syringomyelia, and in syphilitic and tuberculous meningitis. The trunk is occasionally injured in dislocation of the shoulder, although its deeper position and angle of inclination offer a degree of protection not enjoyed by the upper trunk. Nevertheless, its close relation to the first rib renders it especially subject to injury from disease of the rib and the bony anomalies of the lower cervical vertebræ. Thus, cervical rib is not an uncommon source of injury; and while the obstetrical palsies represent a type characteristic of injury to the upper trunk, the symptoms of cervical rib constitute a syndrome distinctive of the lower trunk lesion. Morbid growths in the neck and pulmonary tumors may involve the lower brachial fibres; and Rigaldoni has described an instance in which injury to the trunk, associated with pupillary changes, resulted from metastatic carcinoma of the lungs. Neuritis of the lower trunk has occurred as a complication of influenza, and the lower type of paralysis is sometimes a residual symptom of a complete plexus lesion.

Three important nerves of the brachial plexus are concerned in the formation of the lower trunk; and the clinical symptoms resulting from lesions of this trunk are due to injury to the ulnar, one-half of the median, and a portion of the radial nerves. Occasionally, the spinociliary fibres from the first thoracic segment are implicated, and injury to the phrenic nerve has also been described. Clinically then, the small muscles of the hand, and those of the hypothenar and thenar eminences are paralyzed and atrophic; and when the paralysis affects principally the intrinsic muscles of the hand, the part assumes the characteristic posture known as claw-hand, or *main en griffe*. This condition is also a symptom of syringomyelia and progressive central muscular atrophy. Occasionally, the flexors of the wrist are paralyzed with subsequent contracture of the unopposed extensor muscles; and sometimes the fibres of the seventh cervical root are damaged, so that paralysis of the triceps and extensors of the wrist may be added to the clinical picture. Contraction of the pupil, narrowing of the palpebral fissure, and slight exophthalmos are indicative of sympathetic involvement, and suggest the probability of injury to the nerve root. To these symptoms Macle has added variations in the tension of the brachial artery, and vasomotor disturbances. Variable degrees of sensory loss are usually demonstrable along the ulnar border of the forearm and hand; and these may, according to the studies of André-Thomas, Oppenheim, and others conform to the radicular grouping of the nerve fibres.

**OBSTETRICAL PARALYSIS—DUCHENNE-ERB BIRTH PALSY.**—Obstetricians have used the former term to designate a paralytic disorder occurring either in the mother during the course of pregnancy, or in the child at the time of delivery; but the condition to be described in this section is restricted to the affection as it occurs in the offspring, and, may, therefore, be more suitably designated as the Duchenne-Erb or infantile brachial birth palsy. It has long been recognized that during the mechanism of labor certain infants are born with variable degrees of paralysis of the arm. In 1872 Duchenne determined, by electrical examination, the group of paralytic muscles; but apparently he did not



recognize the nature of the affection. Two years later Erb observed, both in the infant and in the adult, a similar type of palsy with, occasionally, a more extensive muscle involvement. He located the lesion in the upper trunk of the brachial plexus, and also found that, if this trunk were electrically stimulated in the normal individual, a contraction was obtained in the group of muscles usually affected in the birth palsies. The point of stimulation is now known as Erb's point, and has already been described under *Lesions of the Upper Trunk*.

Although clinical and anatomical confirmation of these earlier studies has accumulated, the etiology, mechanism, and even the pathology of the birth palsies continue to be subjects of animated controversy. That the lesion is of traumatic origin and confined largely to the fibres of the upper trunk is generally admitted, but the cause and nature of the injury are not fully determined. Fetal malpositions, anatomical abnormalities in the birth canal, and prolonged or difficult delivery have been thought to be contributing factors. Erb attributed the paralysis to compression or laceration of the trunk, from pressure of the clavicle against the first rib or vertebral process during delivery by the Prague manoeuvre. It has also been claimed that the injury is the result of direct pressure upon the nerve trunk by the fingers of the obstetrician during the management of breech presentation, or from the use of carelessly applied forceps in instrumental deliveries. A more popular theory accounts for the lesion by traction exerted upon the upper roots and trunk, on the side opposite to that upon which the head and shoulder are approximated during the delivery of vertex presentations. Hyperextension of the arm, following breech extraction, is thought to be a source of injury; and, occasionally, fracture of the clavicle or humerus may be a contributing factor. Nevertheless, the studies of Bullock, and of Clark, Taylor and Prout appear to discredit the theory of clavicular pressure, hyperextension of the arm, or instrumental delivery as a satisfactory explanation of the injury. Traction upon the roots or trunk is, in their opinion, a more probable cause. Recently T. T. Thomas has made a further study in support of his theory that the affection is merely a pseudo-paralysis, dependent upon primary injury to the capsule of the shoulder joint or to dislocation of the humeral head. It is claimed that the nerves are only secondarily involved by the axillary inflammation consequent upon the joint or capsular injury. Thomas further maintains that, at first, the entire upper extremity is affected, and that the condition is "not a paralysis limited to the small Duchenne-Erb group of muscles." His position has, however, not been generally accepted, and is rather energetically opposed in the writings of J. J. Thomas and J. W. Sever. Nevertheless, the occasional occurrence of birth palsy in perfectly normal labor has created a belief that whatever may be the mechanism of the direct injury, there is, in all probability, some additional unknown factor.

The character of the pathological changes, which may be found in the nerve trunk, depends upon the nature and extent of the injury. Those who have studied the plexus at different intervals after the development of paralytic symptoms have found lesions varying from compression of the trunk to complete rupture of the nerve fibres; and in cases of long duration the nerves are often imbedded in dense scar tissue. Occasionally, a large, recent, or partly organized hematoma has occupied the clavicular and axillary spaces.

Three clinical types of the affection have been described: First, that due to involvement of the upper roots or trunk with the production of the classical Duchenne-Erb syndrome; secondly, that resulting from a lesion of the lower roots or trunk, with the features of a Klumpke type of palsy; and lastly, a combined palsy of the upper and lower trunks. The last two types are of unusual occurrence; and the symptomatology of the disease is recognized by the previously described features characteristic of lesions of the upper trunk. Thus, it is usual to find paralysis of the deltoid, biceps, brachialis anticus, and brachioradialis muscles. Occasionally, the seventh cervical root is implicated, and the paralysis is then more widespread; so that the extensors of the wrist and fingers are sometimes affected. According to Bullock, the serratus magnus has at times been involved, but it is often difficult to determine the exact extent of the palsy because of the inaccuracies attending the examination of so young a patient.

Usually the paralyzed arm hangs limp at the side of the body; the humerus is rotated inward; and, in some instances, the forearm is pronated to so great an extent that the palm of the hand looks backward and outward. The arm cannot be abducted, and, if elevated, falls immediately to its original position when the support is removed. Supination and flexion of the forearm cannot be performed; but, ordinarily, movements of the wrist and fingers are not greatly impaired. In the earlier stages, atrophy and contracture are not apparent; but in children with a generous supply of subcutaneous fat it is often difficult to detect the presence of atrophy. Stimulation of Erb's point usually fails to produce a response, and the paretic muscles exhibit the reaction of degeneration and subsequent contracture in cases of long standing, or incomplete recovery. Pain is, ordinarily, not a feature of the affection, but insignificant sensory defects have been noted in the distribution of the musculocutaneous and radial nerves.

The prognosis depends upon the damage which the nerves have suffered. In a few instances recovery is spontaneous and comparatively early; but in most cases the affection persists for many months, and not infrequently exhibits a variable degree of residual palsy. A final opinion should, however, be reserved, since an apparently unfavorable condition has terminated in complete recovery after a period of eighteen months or longer.

Treatment should be instituted early. The arm should be placed in a position to relieve tension upon the paralyzed muscles, and for this purpose a sling or suitable orthopedic apparatus may be devised. **Massage and passive movements** may be used to advantage, and **electricity** still has a limited field of usefulness. Upon return of voluntary movement, active, graduated exercise should be prescribed for increasing periods. T. T. Thomas advises immediate attention to the shoulder joint. If recovery is greatly delayed, or incomplete, **surgical intervention** may be advised with the object of freeing the nerves of scar tissue or, if necessary, section and suture.

**CERVICAL RIB.**—Supernumerary rib as an anatomical abnormality is said to have been recognized since the time of Galen, but its clinical importance remained obscure until the appearance of Hunauld's paper, in 1742. More than a century later, Gruber found the clinical records of only 76 cases in the literature; and it is only within the past fifteen

years that the affection has been accorded clinical prominence through the studies of Pilling, Keen, Bramwell, and Sargent.

Abnormalities of the transverse processes are not uncommon, and have been noted on both the cervical and lumbar vertebræ; but the rudimentary rib belongs especially to the cervical region. The anomaly is usually bilateral, but not symmetrical; and although both ribs are attached to the seventh cervical vertebræ, one is generally situated at a slightly higher level, and, usually, is more fully developed than that of the opposite side. Keen has described two additional ribs upon the same side. The origin, direction, and attachment of the rib vary; and, until recently, the classification recommended by Gruber has been generally accepted. Sargent is of the opinion, however, that Gruber's classification does not embrace all of the varieties of rib anomalies, nor does it take into account whether or not the rib is movable. He, accordingly, suggests the following:

"(1) An exaggerated costal process of the seventh cervical vertebra, not joined to but fused with the transverse process, and continued forwards and downwards as a fibrous band to be attached to the first thoracic rib behind the scalene tubercle.

"(2) A short rib, articulated to the seventh cervical vertebra by costocentral and costotransverse joints, and continued onwards as a fibrous band to be attached to the first rib as in Type 1.

"(3) A jointed rib of sufficient length to carry the eighth root upon its bony portion, and attached by a fibrous band to the first rib.

"(4) A jointed rib of which the anterior extremity makes contact with the first thoracic rib; the two being either fused, or united by an irregular articulation.

"(5) A rudimentary first thoracic rib, the anterior fibrous portion of which is attached to the sternum, usually by a rudimentary costal cartilage."

The relation of the rib to the surrounding structures is important. According to Keen the subclavian artery is invariably situated above, but not necessarily resting upon the rib. Occasionally, the vessel passes anterior to its free end; and when the artery lies directly over the rib, the lower nerve trunk always takes a similar course.

At times the dome of the pleura is adherent to the body, or fibrous prolongation of the rib. There is some evidence that the prefixed type of plexus and cervical rib are commonly associated, and that the post-fixed plexus is accompanied by abnormalities of the first thoracic rib; but Sargent finds no constant relationship between the two anomalies. Not infrequently, cervical rib has been noted in conjunction with a normally fixed plexus.

Compression of the lower cervical nerves may result from bony abnormalities other than those connected with the seventh cervical vertebræ. Thus, a rudimentary or abnormally developed first thoracic rib, diseases of the rib, and, according to Cadwalader, bony growths of the upper thorax have produced the symptoms of cervical rib; and, occasionally, a normal first rib has been the cause of pressure in the post-fixed type of plexus. Ordinarily, the rib anomalies are not accompanied by other congenital abnormalities. Keen, however, reports the occurrence of cervical rib associated with imperforate vagina, club-foot, scoliosis, progressive central muscular atrophy, syringomyelia and multiple sclerosis; but disseminated sclerosis is now regarded as an inflammatory rather than a developmental disorder.

*Clinical Characteristics.*—Cervical rib, although a congenital abnormality, is rarely productive of symptoms during childhood. Not infrequently, the anomaly exists throughout life without causing any

disturbance of function, and may thus be discovered only accidentally. The condition is more common in the female. In Keen's 42 cases, 31 were in women, while in Trostler's series of 65 cases, 45 were in the female.

The statistics of Keen, Bramwell and Dykes, Sargent, and Trostler give thirty-five years as the average age for the first appearance of pressure symptoms, although evidence of the disease has been noted as early as four and a half years, and as late as the sixth decade. For a time, the symptoms may be mistaken for neuritis or some other disorder; and Trostler finds a period, varying from a few months to fifteen years, in which evidences of the affection had been noted. Notwithstanding the frequent bilateral occurrence of the abnormality, the symptoms, are, as a rule, unilateral, and more common upon the right side.

*Causes of the Symptoms.*—According to Keen, only 5 or 10 per cent. of the cases of cervical rib are accompanied by clinical evidences of a nerve lesion. Hence, the late appearance or absence of symptoms, the greater frequency of the right-sided affection, and its more common occurrence in the female are features which cannot be explained by the mere presence of a supernumerary rib. The late appearance of symptoms has been attributed by Murphy to the downward and progressive growth of the rib, but this theory does not account for the development of the condition after the full adolescent period. Keen suggests as contributing factors, the arterial changes, muscular atony, and drooping of the shoulder consequent upon advancing age; while the thoracic type of respiration in the female is said to account for the greater frequency of the affection in women, and the more active use of the right arm, for the predominance of symptoms on that side. Plummer is of the opinion that in one of his cases the affection was initiated by a cervical adenitis.

Certain forms of occupation, abnormal position of the arm, and trauma are not infrequent causes of the initial symptoms. Thus, a fall upon the shoulder or the outstretched arm, a slight misstep, overexertion, and the lifting of heavy objects have preceded the onset of the disorder in many instances. Pianists, bookkeepers, postmen, seamstresses, telegraphers, and typists are sometimes affected from continued use of the arms, or from pressure upon the neck and shoulder incident to the nature of the occupation. Perhaps abnormal positions of the arm, or undue pressure upon the neck during surgical anesthesia are occasional inciting factors; and anemia, nutritional disorders, and cachectic states, with loss of weight and subsequent drooping of the shoulders, have been mentioned as predisposing agents. Occasionally, the symptoms have developed during the course of diphtheria and influenza.

*Symptomatology.*—The affection usually manifests itself by evidences of irritation or interruption of the nerve fibres constituting the seventh or eighth cervical roots. Thus, following a slight injury, a period of overwork, or perhaps without any apparent cause, pain, tingling, and numbness are experienced along the ulnar border of the forearm, in the little finger, and a portion of the ring finger. Occasionally, the entire arm is painful or weak, and undue fatigue, and awkwardness in using the hand may precede the onset of the sensory symptoms. Usually, the pain is of the neuralgic type, sharp, shooting in character, and may radiate from the neck downward, or from the fingers to the arm, shoulder, neck, or head. Movement and dependent positions of the arm increase the suffering, which may often be relieved by hyperextension

and support of the extremity. Not infrequently, circulatory, vasomotor, and sympathetic disorders are added to the symptomatology.

(a) *Sensory Symptoms*.—Subjective sensations of pain, paresthesia, and numbness are usually referred to the distribution of the ulnar or the median nerve; and, objectively, there may be impairment of all forms of cutaneous sensibility, although complete anesthesia is not a common feature. In some instances, sensory disorders are noted in the distribution of the radial nerve, and Wilson attributes them to involvement of the sixth cervical root in the postfixed type of plexus. One of the author's patients suffered from pain, confined almost entirely to the radial distribution, and a loss of epieritic sensibility over the dorsum of the thumb and index finger. The ulnar nerve was apparently unaffected, but the radiogram disclosed a well-marked cervical rib. The sensory changes due to rib pressure have been carefully studied by Barker, Patrick, and Bernhardt, who have occasionally found total anesthesia in the ulnar area. In Patrick's case the sensory loss was such that the patient accidentally burned the anesthetic area without experiencing any sensory discomfort.

(b) *Motor Symptoms*.—Weakness, paralysis, atrophy, and the reaction of degeneration are the common features, although the motor fibres are not invariably affected. S. A. K. Wilson has described a special type of muscular wasting in the distribution of the median nerve, in which paralysis of the abductor brevis pollicis and the opponens pollicis is of particular interest. The remaining muscle of the thenar group, the flexor brevis pollicis, innervated also by the median nerve is not affected; and Wilson concludes that this muscle receives its fibres from the eighth cervical segment which, ordinarily, is not implicated in the median type of rib palsy. This selective atrophy of the thenar muscles is, in his opinion, of diagnostic value, and serves to distinguish the median atrophy of rib pressure, from the "global" atrophy of the progressive central lesion in which the entire thenar eminence is involved. Cervical rib is the cause of a second type of atrophy affecting principally the fibres of the ulnar nerve, with resulting paralysis of the interossei and the development of the characteristic "claw-hand." Occasionally the paralysis involves the muscles of the shoulder and arm, and Keen refers to hysterical dysphagia as an associated motor disturbance.

(c) *Sympathetic, Vasomotor, and Trophic Disorders*.—Coldness, pallor, cyanosis, and, more rarely, edema of the hand and arm have been noted, but vasomotor disturbances are, as a rule, of infrequent occurrence. Colonna has described vascular symptoms resembling those of Raynaud's disease. The skin may be moist or dry, and Keen has observed trophic changes in the nails. It is often claimed that the cervical sympathetic is not involved, but Sargent describes myosis and widening of the palpebral fissure as evidences of injury to this system of fibres. Symptoms of this character and the occasional harshness of the voice are, however, usually attributed to an associated syringomyelia.

(d) *Vascular Disorders*.—Both local and distant changes have been noted in the larger blood-vessels. A visible or palpable tumor is not infrequently present in the supraclavicular region. The mass may be movable or attached to the surrounding parts, and, occasionally, pulsation, a thrill, or a systolic bruit may be detected. In some instances, when the arm is in the dependent position, the pulse is obliterated in the axillary, brachial, radial, and ulnar vessels; but the circulation is soon

reestablished upon elevation of the extremity. Gangrene is a rare complication.

*Diagnosis.*—Usually, the diagnosis is not difficult. In the typical case, tenderness, local swelling, and pulsation above the clavicle, sensory or motor disturbances in the distribution of the lower cervical roots, and the x-ray serve to determine the nature of the affection. Notwithstanding the presence of a supra-clavicular tumor in all of Henderson's 31 cases, the discovery of a palpable mass, subclavian pulsation, or a systolic bruit in the supraclavicular fossa is not necessarily diagnostic of cervical rib. Occasionally, the first thoracic rib is palpable above the clavicle, and a pulsating tumor may be entirely independent of the bony anomaly. Even the x-ray may be misleading, since the shadow depends largely upon the direction and character of the new growth; and failure to detect the presence of a rib by this means is no proof of its absence. A fibrous band, an abnormal first rib, or a normal first rib in conjunction with the postfixed type of plexus sometimes produce the symptoms of cervical rib; but these conditions may not be demonstrable in the radiogram. In the differential diagnosis, it is necessary to distinguish the affection from neuritis, neuralgia, and writers' cramp; but in these conditions the paralysis is not of the radicular type; the sensory and motor symptoms are more diffuse; the pain is more continuous; and nerve tenderness and muscle spasm are additional features. The selective paralysis of the thenar muscles is an important sign in distinguishing the motor symptoms of cervical rib from those of progressive central muscular atrophy; and, moreover, pain and sensory disorders do not belong to the latter disease. Atrophy of the intrinsic muscles of the hand occurs also in syringomyelia, but there are in addition, evidences of a spinal cord lesion, dissociation of sensation, and, more frequently, the manifestation of sympathetic involvement.

*Treatment.*—From the very nature of the affection it would seem that the only rational therapeutic procedure must be some form of **surgical intervention**. Nevertheless, it is well to adopt, in the beginning, more conservative measures. Since the lesion is essentially a traumatic radiculitis much benefit is to be derived, as in most nerve injuries, from **complete rest and immobilization** of the affected part. The arm should be elevated and supported upon a pillow, or carried in a sling when the patient is not confined to bed. Later, **massage, soothing liniments, electricity, and douching** are of service; and, if the pain is severe, **anodynes**, with the exception of opium, may be prescribed for a brief period. Cachectic, anemic, and metabolic disorders require appropriate therapy; and, when a particular occupation is a contributing factor, a change of employment should be recommended. If these simpler measures fail to secure relief, or if there be recurrent attacks upon the resumption of active life, it may then be well to advise a more radical form of treatment. The results of surgical intervention are, in most instances, quite satisfactory; but the patient should be informed of the probability of more extensive injury to the lower brachial nerves during the course of the operation. Protection of the paralyzed muscles, massage, and electricity are important measures in the postoperative therapy.

**The Posterior Thoracic Nerve (C. 4, 5, 6, 7).**—The nerve, known also as the long thoracic, or external respiratory nerve of Bell, is derived, ordinarily, from the fifth and sixth cervical roots before they have united

to form the upper trunk of the brachial plexus. Occasionally, communicating branches are received from the fourth and seventh cervical nerves. The radicular filaments, after uniting within the substance of the scalenus medius, emerge as a long nerve trunk for the innervation of the serratus magnus muscle. This muscle arises by nine digitations from the upper eight ribs, and is inserted upon the ventral aspect of the vertebral border of the scapula which is thus held closely applied to the thoracic wall. Contraction of the serratus draws the scapula forward and lateralward, with elevation and slight rotation of its vertebral border; but the serratus function is, however, counteracted to some extent by the action of the rhomboids, and the levator anguli scapulæ. Ordinarily, the muscle serves to fix the scapula to the thoracic wall, and thus permits abduction of the arm above a right angle; but when not functioning in this capacity, it becomes an important accessory respiratory muscle.

**PARALYSIS OF THE NERVE.**—Isolated paralysis of the long thoracic nerve is uncommon. According to Osler, Steinhausen in 1900 found the records of only 29 instances. Camp has since reported its involvement following an operation for cervical adenitis, and Besley has observed paralysis confined to the serratus magnus resulting from a local inflammatory disease of the nerve.

More often, the paralysis is part of a multiple nerve lesion; and the affection is said to occur with greater frequency in the male, and more commonly upon the right side. The lesion is usually the result of injury to the nerve in the neck, or more rarely in the axilla. Thus, stab, or gunshot wounds of the lower cervical region, the pressure of heavy objects carried upon the shoulders, overexertion, and the sudden contracture of the scalenus medius have resulted in paralysis of the serratus magnus. Occupations which necessitate excessive and prolonged hyperextension of the arms, such as that required of linemen and ceiling painters, are important etiologic factors, and probably account for the greater frequency of the affection in the male. Occasionally the nerve is affected as part of a multiple neuritis, or as a mononeuritis in influenza, diphtheria, typhoid fever, and infectious arthritis; and a serratus palsy of rheumatic origin has been recorded. Gowers describes the affection as a postpartum complication; and paralysis of the serratus is a not infrequent symptom of progressive muscular atrophy, poliomyelitis, and the muscular dystrophies.

**Symptomatology.**—The evidences of injury or disease of the long thoracic nerve are due to the paralysis of the serratus magnus muscle, with the production of the characteristic "winged" scapula. At rest, with the arm hanging by the side, there may be little or no evidence of the deformity; but close inspection usually discloses slight inward rotation and elevation of the scapula, and recession of its inferior angle from the thoracic wall. Although there is moderate weakness of the extremity, the most obvious defect is noted when the patient attempts to abduct the arm above a right angle. Notwithstanding the partial fixation of the scapula by the middle fibres of the trapezius, this movement can be only imperfectly accomplished; but if the examiner hold the scapula firmly against the thorax a surprising degree of additional movement may be attained. The "winged" scapula is more readily demonstrated by having the patient push, with the extended arm, against a

fixed object, when it will appear as if the lower angle of the scapula might protude through the overlying soft parts. Guillain and Vibert have directed attention to certain changes in the lower part of the neck, which they designate as the "sign of the supraclavicular fossa." When the patient attempts to elevate or shrug the shoulder, it will be noticed that the supraclavicular fossa on the affected side has lost its triangular outline; it is narrower in its lateral measurement and shallower, and more trough-like than on the sound side. As a rule, there are no objective sensory disturbances, but when the paralysis is of neuritic origin there may be pain in the neck, shoulder, or arm. In severe cases, the muscle exhibits the reaction of degeneration.

**TREATMENT.**—Recovery is often slow, and in some instances the paralysis may be permanent. Return of function is encouraged, however, by **keeping the arm at rest, and supported in a sling** so adjusted as to slightly elevate the shoulder. Movements, which necessitate overaction of the scaleni, are to be avoided. If pain is a feature of the disorder, **rest in bed**, and the measures ordinarily employed in the treatment of neuritis are to be prescribed; and later, **galvanic stimulation** of the muscle may be used to advantage. Neumeister has devised a mechanical support for the shoulder which is apparently of therapeutic value. Two scapular pads, connected by a metal bar, are attached by axillary and shoulder straps, to a horizontal iron bar across the chest. By this means sufficient pressure is exerted upon the scapula to approximate its normal position, and consequently the patient is enabled to use the arm more freely, and with the least degree of injury to the muscle.

**The Suprascapular Nerve (C. 4, 5, 6).**—The deep position and comparatively short course of this nerve protect it from the usual forms of injury, and only rarely is it the seat of disease. The trunk arises from the supraclavicular portion of the brachial plexus and is formed by a portion of the fifth and sixth cervical roots, but occasionally a branch is contributed from the fourth cervical. Terminal branches innervate the supraspinatus and infraspinatus muscles, and a small filament is distributed to the shoulder joint. Its sensory distribution is not well defined.

The supraspinatus is a thick triangular muscle arising from the supraspinous fossa of the scapula to be inserted into the upper facet of the great tubercle of the humerus, where it fuses with the capsule of the shoulder joint. Its action is to lift the arm lateralward, to help maintain the position of the humeral head, and to feebly rotate the humerus inward. The infraspinatus, a similarly shaped muscle, originates from the infraspinous fossa and is inserted into the middle facet of the great tubercle of the humerus, and capsule of the shoulder joint. It acts principally as an external rotator of the arm.

Paralysis of the suprascapular nerve may be the result of fracture or dislocation of the shoulder, contused or incised wounds of the neck, or a fall upon the shoulder or outstretched arm. Starr has seen it injured during an operation for cervical adenitis; and, rarely, it may be the seat of a true mononeuritis although it is more frequently involved in conjunction with the circumflex.

Clinically, suprascapular palsy causes slight impairment in the use of the entire arm, but more particularly in the movements of abduction and external rotation. There is, accordingly, some difficulty in writing;



and, when the arm is raised to a right angle it cannot be maintained in this position, because of slight relaxation of the capsule of the shoulder joint and consequent lowering of the humeral head. The scapula may be slight rotated, with resulting prominence of its upper angle; and finally, in prolonged cases, the affected muscles undergo atrophic and degenerative changes. The scapular spine, thus, becomes more prominent from the resulting depression in the supra- and infra-spinous fossæ. Occasionally, a small area of cutaneous anesthesia has been demonstrated over the scapular and posterior deltoid regions.

Surgical repair of the contused or divided nerve is especially difficult because of its inaccessibility, but inflammatory and degenerative lesions of the trunk generally respond to the therapeutic measures adopted in the treatment of neuritis. If possible, the exciting cause should be removed, and the nutrition of the muscle maintained by massage and electricity. A support for the shoulder and arm may be used to advantage.

**The Axillary or Circumflex Nerve (C. 5, 6).**—This, the smaller of the two terminal branches of the posterior cord of the brachial plexus, is formed by the union of fibres from the fifth and sixth cervical roots. The nerve innervates the deltoid and teres minor muscles, the shoulder joint, and the skin over the posterior part of the deltoid muscle and in a small area over the posterolateral aspect of the arm. The deltoid arises from the acromion, the outer portion of the clavicle, and the spine of the scapula, and is inserted into the deltoid tuberosity of the humerus. When the entire muscle contracts the arm is abducted; but if the contraction is limited to its anterior portion, the arm is abducted and brought forward, while contraction of the posterior fibres alone produces abduction and backward movement of the extremity. The teres minor, attached to the dorsum of the scapula and great tuberosity of the humerus, rotates the arm outward, and when acting in conjunction with the deltoid permits a greater degree of abduction by the latter muscle.

The axillary nerve is seldom paralyzed alone. Benisty does not record a single instance among several hundred cases of traumatic lesions of the brachial nerves. The nerve, together with the suprascapular, is most frequently injured from falls or blows upon the shoulder, and dislocation or fracture of the humerus. Axillary paralysis has, however, been observed as part of a crutch palsy, from pressure during ether narcosis, and as the result of certain kinds of occupation. It is said not to be uncommon in miners, whose occupation often necessitates a cramped, reclining posture in which the shoulder is subjected to continuous pressure for prolonged periods. A bilateral isolated paralysis of the nerve has been described. Occasionally, the nerve has been affected in lead poisoning, diabetes, typhoid fever, and as a postpartum complication in the mother. Excessive muscular action and extreme hyperextension of the arm, during sleep, have resulted in paralysis of the deltoid.

Destructive lesions of the axillary nerve produce complete paralysis of the deltoid and teres minor muscles and, very often, a loss of protopathic and epicritic sensibility on the posterior aspect of the arm from the acromion to a level slightly below the insertion of the deltoid. The onset of the paralysis is sometimes accompanied by pain in or about the shoulder joint. Voluntary abduction of the arm is quite impossible except, to a slight degree, by forcible contraction of the trapezius, serratus magnus,

and supraspinatus muscles. As atrophy develops, the shoulder becomes flattened; the bony parts more prominent; and, later, there is relaxation of the joint. The muscles soon exhibit the reaction of degeneration which may serve to distinguish the neural from the arthritic type of atrophy. In paralyses of long-standing the other muscles about the shoulder often undergo marked hypertrophy, and there may be a moderate degree of ankylosis of the joint. Unless the nerve has been completely severed, the outlook for recovery is good; but, occasionally, it may become necessary to resort to muscle grafting or suprascapular-axillary anastomosis.

**The Radial or Musculospiral Nerve (C. 5, 6, 7, 8; T. 1).**—The radial, the largest nerve of the brachial plexus, is derived principally from the sixth, seventh, and eighth cervical roots, but very often receives communicating filaments from the fifth cervical and first thoracic nerves. The trunk forms the chief terminal division of the posterior cord, and conveys muscular, articular, and cutaneous branches to the arm, forearm, and hand. Motor fibres are distributed to the following muscles: triceps, brachioradialis, extensor carpi radialis longior, anconeus, extensor carpi ulnaris, extensor carpi radialis brevior, extensor communis digitorum, abductor longus pollicis, and extensor brevis pollicis. Thus the nerve innervates, principally, the extensor muscles of the forearm, wrist, and fingers. Cutaneous sensory fibres are conveyed to the posterior and lateral aspects of the arm, forearm, and hand.

The study of nerve lesions during the World War has revealed some interesting anatomical and physiological peculiarities of the radial nerve. Like the median, it appears to possess a certain individuality. It is particularly vulnerable; it recovers from injury in a characteristic fashion; and, although a mixed nerve, it is largely motor in function. Marie, Meige, and Gosset have determined the pattern of the motor fibres, and find that those situated in the anterolateral portion of the trunk are distributed to the two radial extensors of the wrist; those in the postero-internal portion are conveyed to the extensors of the fingers; while those occupying a distinct lateral position are concerned in the movement of supination.

**PARALYSIS OF THE NERVE.**—Traumatic lesions of the radial nerve are especially common, although the studies of White, Fisk and Broek give a higher percentage of injuries to the median and ulnar nerves during the recent war. In civil life, however, the radial lesion occurs with greater frequency. The nerve may be injured in the axilla, from fracture or dislocation of the humerus, and crutch paralysis in this situation is not uncommon; but there is more likelihood of injury at the junction of the middle and lower thirds of the arm. Here, the nerve becomes more superficial and exposed to damage from stab or incised wounds, and pressure of various sorts. Reference has already been made to the "Saturday-night arm" occurring in alcoholic stupor; and in profound natural sleep, with the head resting on the arm, sufficient pressure may be exerted to produce a complete wrist-drop. Application of the Esmarch bandage, the injection of sera, and violent muscular contraction are additional causes of radial paralysis; and radial neuritis from exposure or of rheumatic origin has been described. It is well-known that lead appears to have a particular affinity for the nerve; but lead palsy is usually bilateral and distinguished by escape of the brachioradialis. Preservation of function in the muscle may be readily determined by having

the patient flex the forearm against resistance, when the edge of the supinator may be obvious and palpable at the bend of the elbow.

*Symptomatology.*—The symptoms depend upon the nature, extent, and location of the injury. When the nerve is severely damaged in the axilla there is complete paralysis of the triceps, supinator longus, and all the extensor muscles in forearm and hand. The forearm is pronated and slightly flexed, and the hand assumes the position characteristic of wrist-drop. Extension of the forearm, wrist, and fingers is lost, and supination is greatly restricted. The fingers are partially flexed, but do not show, in the beginning, any evidence of contracture.

Injury to the nerves is relatively common in the lower part of the arm where it becomes more superficial as it follows the radial groove of the humerus. Since the fibres to the triceps muscle leave the nerve at a higher level, lesions in this situation do not, as a rule, interfere with extension of the forearm; and not infrequently the supinator longus also escapes. In case the latter muscle is involved supination cannot be performed so long as the elbow is extended; but, with the forearm flexed, contraction of the biceps and rotation of the humerus serve to complete the movement of supination. Wrist-drop is, however, pronounced, and abduction and extension of the thumb are impossible. Because of the dependent position of the wrist and loss of synergistic action in the extensors, there is apparent weakness of the flexors of the fingers when the patient attempts to grasp the examiner's hand. There is, of course, no real weakness of the flexor muscles; but a vigorous grasp of the hand can be accomplished, only, when the extensors are simultaneously contracted. When the nerve is injured in the forearm, the supinator and the extensors of the wrist escape. In cases of long standing, the reaction of degeneration and atrophy make their appearance; but the electrical examination may be misleading unless the nerve is stimulated at various levels. This is due to the observation, previously referred to, that certain lesions appear to inhibit the passage of the nerve impulse, or the electric current without causing degeneration of the nerve. Hence, stimulation above the point of injury may fail to produce a response, while a good contraction may be obtained by stimulation at a lower level. Trophic disorders are said to be rare. From the dependent position of the hand and relaxed condition of the joint, the wrist is often unduly prominent, and effusion into the joint and ankylosis have been described. André-Thomas refers to loss of the pilomotor reflex.

Three well-defined sensory branches are derived from the radial nerve: The internal cutaneous, which arises in the upper part of the arm, and innervates the skin on the posterior aspect of the arm from the insertion of the deltoid to the olecranon; the external cutaneous, distributed to the integument on the postero-external aspect of the forearm, arises in the lower third of the arm; and the superficial radial nerve, which leaves the radial main trunk just below the bend of the elbow and is distributed to the half of the dorsum of the hand. Notwithstanding this extensive cutaneous innervation, the sensory disturbances incident to radial palsy are often indefinite, and very frequently absent. Hamilton, in a study of 55 cases of radial nerve paralysis, found the detection of sensory loss quite unsatisfactory and indefinite. Nevertheless, in many instances, there was a variable degree of sensory defects particularly constant on the posterior aspect of the arm and the dorsum of the hand. He attributes the anomaly to the over-lap of adjacent cutaneous nerves, although

White does not concur with this opinion. The protopathic and epicritic fields of sensory loss are said to show a fairly constant, but disproportionate relation, in which there is generally a distinct over-lap of epicritic defect. The full extent of the anesthetic field can be determined only by examination with the lightest tactile impressions. Pressure sense and pain sense are very slightly affected, and confined to a restricted area over the thumb, first interosseous space, and the first phalanges of the index and middle fingers. Deep sensibility is said not to be affected, and the preservation of these fibres is thought to explain the frequent absence of pain and other subjective sensory disturbances. Only occasionally is there more than a vague sensation of numbness or tingling in the first interosseous space and over the radial half of the back of the hand.

*Diagnosis.*—The studies of Benisty have shown that paralysis of the radial nerve is not infrequently simulated by other diseases of the upper extremity. Thus the "congealed hand," described by Meige, resembles very closely the radial lesion, but in the former condition, the wrist-drop is not so pronounced; the fingers are rigid instead of flaccid; and the electrical reactions are normal. Occasionally, direct injury to the extensor muscles, fibrous adhesions, and vascular lesions of the tendons or bones may be the cause of a partial wrist-drop. Painful affections of the median nerve, with protective voluntary contraction of the flexor muscles, and the hysterical contractures sometimes resemble a true radial paralysis. Because of certain deceptive muscular movements, to which Woods has directed attention, it is, at times, difficult to determine the degree of motor paralysis. Woods finds that in some instances of complete lesion of the radial nerve there are, following relaxation of the firmly closed hand, occasional feeble extensor movements of the wrist. These, he attributes to the elastic rebound of the joint due to the withdrawal of tension to which the soft parts and extensor tendons were subjected during the contraction of the flexor muscles.

*Treatment.*—**Rest, massage, electricity, and relaxation of the parietic muscles** are the essential measures. Clarke and Spriggs have made a special study of various positions of the wrist to determine in which one the greatest degree of relaxation is attained. They find that the best results are secured when the hand is flexed dorsally with the fingers fully extended; but fixation in this position is uncomfortable, so that moderate flexion of the fingers is permitted. Relaxation is to be supplemented by **electricity and passive movements.**

*Prognosis.*—Slight lesions of the nerve recover rapidly; and even in severe injuries, the results of suture are said to be especially favorable, since the preponderance of motor fibres insures more accurate preservation of the nerve pattern and reduces the probability of harmful intermingling of the sensory and motor axones. Restoration of function occurs earlier and to a greater degree when the lesion is situated near the origin of the muscular branches. Since the principal motor nerves leave the radial trunk at the bend of the elbow, the prognosis, in general, depends upon the proximity of the lesion to the lower end of the humerus. The restoration of motor function appears to follow a definite order, and Williams has determined the following sequence of muscle recovery: First, the radial extensors, in from three and a half to eight months; second, the extensor communis digitorum, in from five to twelve months; and lastly, the extensor longus pollicis, in from six to fourteen

months. The progress and degree of recovery may be determined by having the patient hold the hand in the "oath" position. If, in this position, the thumb is extended and the grip is of good quality, recovery is said to be complete; if recovery is only partial the thumb is flexed, and efforts to grasp an object result in a reappearance of the wrist-drop. Pitres has devised another test of functional recovery. He pronounces the recovery complete when the patient, standing erect, can place the little finger on the seam of the trousers, with the remaining fingers fully extended and the palm of the hand turned forward—applicable only to the male.

**The Musculocutaneous Nerve (C. 5, 6, 7).—**Originating from the fifth and sixth cervical roots, and occasionally from the seventh root also, the nerve trunk forms one of the two terminal divisions of the outer cord of the brachial plexus. It innervates the coracobrachialis, the biceps, and the brachialis anticus muscles, and conveys sensory fibres to the integument on the outer half of the flexor surface of the forearm. Isolated paralysis of the nerve is unusual, but it is not infrequently injured in conjunction with the median and the radial and in lesions of the brachial plexus. Incised and contused wounds of the arm, and fracture and dislocation of the humerus are the more common sources of injury. A complete lesion of the nerve produces total paralysis of the coracobrachialis and biceps muscles, and partial paralysis of the brachialis anticus. Thus, when the forearm is supinated, flexion at the elbow cannot be accomplished; but if the forearm be pronated and the radial nerve uninjured, a considerable degree of flexion may be attained through contraction of the brachioradialis. The parietic muscles soon atrophy, and exhibit the reaction of degeneration. The sensory disturbances are characterized by pain, paresthesia, hypesthesia, or anesthesia; and causalgia is sometimes a distressing symptom.

**The Median Nerve (C. 5, 6, 7, 8; T. 1).—**Fibres from the fifth, sixth, seventh, and eighth cervical, and first thoracic roots contribute to the formation of the median nerve. The axones from the three upper roots and those from the two lower roots enter into the formation of the nerve trunk by two branches derived, respectively, from the outer and the inner cords of the brachial plexus. The median nerve then occupies a protected position throughout most of its course and conveys sensory, motor, trophic, and vasomotor fibres to the forearm and hand. In its internal anatomy and physiology, and in its reaction to disease the nerve resembles very closely the sciatic.

With the exception of fibres to the pronator radii teres and to the elbow joint, no branches arise from the nerve in its course through the arm. The principal motor branches leave the trunk a short distance below the elbow and are distributed to the following muscles: Flexor carpi radialis, palmaris longus, flexor sublimis digitorum, flexor longus pollicis, flexor profundus digitorum, the two outer lumbricales, the pronator quadratus, and most of the muscles of the thenar group. Thus the nerve is concerned chiefly with pronation of the forearm, flexion of the wrist and fingers, and opposition of the thumb. Sensory fibres innervate the integument on the outer half of the palm of the hand, the palmar aspect of the thumb, the index and middle fingers, and the radial half of the ring finger. On the dorsal surface of the hand, the skin over the two distal phalanges of the second and third fingers is also in median territory. Anastomotic branches are contributed to the musculocutan-

eous nerve in the arm, and to the ulnar nerve in the palm. During the World War, many opportunities were offered for a study of the median nerve in various lesions, and the observations of Marie, Meige, Benisty and others have added much to the knowledge of its internal structure. These studies have furnished convincing evidence that the motor fibres occupy a fairly constant position within the nerve trunk. Thus, in general, the medial portion of the nerve contains the fibres for the flexors of the fingers, and the anterior portion conveys those distributed to the thenar group of muscles. The fibres to the pronator radii teres are situated in the lateral portion of the nerve trunk, while the sensory pathway occupies the central region.

**PARALYSIS OF THE NERVE.**—Lesions of the median nerve are comparatively uncommon in civil life, but during military engagements they rank next in frequency to those of the radial and ulnar. In civil life the nerve is not infrequently injured in the axilla from fracture and dislocation of the humerus, stab or incised wounds, callous formations, and occasionally from crutch pressure. Prolonged use of the Esmarch bandage is sometimes a cause of median palsy, or the nerve, together with the ulnar, may be injured by incised wounds at the wrist or in the palm. An occupation neuritis of the median and ulnar nerves sometimes develops in cigar and cigarette makers, milk-maids, joiners, dentists, tailors, and washerwomen; but the exact nature of the affection is unknown. A mononeuritis of the median nerve is unusual, but ulnar and median neuritis have occurred during the course of pregnancy and, occasionally, the fibres of the median are involved in cervical rib.

**Symptomatology.**—Injuries of the median nerve are divided by Benisty into two clinical types—the painful and the painless affections. The first type is characterized by a group of symptoms designated by Weir Mitchell as *causalgia*, and described elsewhere in this chapter, under that title. The painless affection is further divided into those resulting from a total lesion of the nerve, and those due to partial or dissociated injuries.

In total paralysis of the nerve, the forearm may rest in extension, or assume a flexed, semi-pronated position. The hand appears to be broader than normal, because of flattening of the thenar eminence and lowering of the thumb to the same plane as that occupied by the other four fingers, thus producing the condition known as the “ape-hand.” At the same time the hand is inclined slightly to the ulnar side. Flexion of the wrist is greatly impaired, and pronation is impossible, except for slight passive execution of this movement when the patient, with the elbow elevated, flexes the forearm and rotates the humerus inward. The index and middle fingers may be slightly hyperextended; the grip of the hand is abolished; the thumb cannot be opposed to the other fingers, or flexed at its distal phalanx; and abduction of the thumb is defective. Flexion of the fingers at the metacarpophalangeal joint is performed by the interossei, which are innervated by the ulnar nerve. This movement is, accordingly, preserved. The second and third phalanges of the little and ring fingers also may be feebly flexed, since the ulnar half of the flexor profundus digitorum receives its motor fibres from the ulnar nerve; but flexion of the remaining fingers, and particularly the second phalanx of the thumb, cannot be performed. The palmar tendons are flattened and remain motionless when the wrist is partly flexed by the action of the flexor carpi ulnaris. Atrophy of the thenar group appears early and,

in long-standing paralysis, the muscles attached to the outer condyle of the humerus become atrophic and show the reaction of degeneration.

The objective sensory changes are variable in degree, quality, and distribution. Generally, the thumb and index fingers show the greatest sensory defect, which, in combination with the motor paralysis, renders them almost completely useless. The epicritic loss is usually more extensive than the protopathic and involves the radial half of the palm. Occasionally, the anesthesia is confined to the second and third phalanges of the index and middle fingers on both their palmar and dorsal aspects, and, at times, hypesthesia is noted on the radial half of the ring finger. The sense of position and the vibratory sense are sometimes lost in the index finger, and stereognosis may be defective. The sensory defect is said to be more pronounced when there is an associated vascular lesion. Vasomotor, secretory and trophic disorders are uncommon; but, occasionally, the hand may be discolored, cyanotic, dry and scaly, and the nails may show trophic changes. These symptoms are, however, more commonly associated with incomplete lesions of the nerve. André-Thomas finds the idiomuscular response to mechanical stimulation greatly prolonged.

In partial or dissociated lesions the internal aspect of the nerve trunk appears to suffer most frequently. Thus, the pronators and flexors of the wrist are only slightly affected, but the flexors of the index finger and thumb usually suffer to a marked degree. The sensory disturbances are mostly of a subjective nature, characterized by vasomotor and secretory changes and, occasionally, the symptoms of causalgia. When the nerve is injured at the wrist the small muscles to the thenar group usually escape, since the motor fibres of these muscles leave the trunk of the median in the lower part of the forearm.

The *prognosis* in median nerve injuries depends upon the extent and character of the lesion, the loss of nerve substance, and the development of scar tissue or callous formation. In the neuritides and pressure palsies, the outlook is generally favorable. Ordinarily, return of sensory function precedes the recovery of voluntary motion, although stereognostic loss may persist over a prolonged period. The muscles are said to recover in the following order: First, the pronator and palmar muscles; next, the flexors of the middle finger and the thumb; and lastly, the flexors of the index finger and the small muscles of the thumb. According to Benisty, paralysis of the thumb may persist for two years or more, or it may even be permanent. Treatment of the palsy is, in general, similar to that adopted in injuries and disease of the other spinal nerves.

**The Ulnar Nerve (C. 7, 8; T. 1).**—Formed largely from the eighth cervical and first thoracic roots, the nerve is derived from the lower trunk, and leaves the plexus as a branch of the inner head of the median. There is some evidence that it receives fibres also from the seventh cervical root, since Testut has described a lesion involving the eighth cervical and first dorsal segments of the spinal cord, with preservation of function in a portion of the ulnar distribution. No important branches arise from the nerve in the arm. Its motor fibres are distributed to the flexor carpi ulnaris, the inner half of the flexor profundus digitorum, and, through the palmar branch, to the two inner lumbricales, all the muscles of the hypothenar eminence, all of the palmar and dorsal interossei, the adductor pollicis, the inner head of the flexor brevis pollicis,

and the palmaris brevis. Sensory fibres are conveyed to the skin on the ulnar-dorsal aspect of the hand, the dorsum of the little finger, and part of the ring and middle fingers. The nerve, thus innervates most of the intrinsic muscles of the hand, and the integument of the hypothenar eminence, the little finger, and half of the ring finger.

**PARALYSIS OF THE NERVE.**—Lesions of the nerve, either alone or in combination with other nerves, have resulted from fracture or dislocation of the humerus, injuries at the elbow, callus formations and, occasionally, from the use of crutches. Not infrequently, minor ulnar symptoms have been due to pressure upon the nerve from abnormal positions of the arm during sleep, but the nerve is more commonly injured in contused or incised wounds at the wrist and elbow. With the exception of the leprosy form, isolated ulnar neuritis is rare. Reference has already been made to the development of ulnar palsy following the administration of antityphoid serum, which, from the patient's statement, must have been injected directly into the nerve trunk. Gibson has described an occupation ulnar neuritis attributed to the long-continued skinning of hides.

**Symptomatology.**—The nerve may suffer a total or a partial paralysis. Its complete division causes marked wasting of most of the intrinsic muscles of the hand and, according to Benisty, particularly those in the first dorsal interosseous space. When the injury is inflicted at the elbow, voluntary flexion of the wrist is defective, but André-Thomas finds that a greater degree of passive flexion is possible, because of the paralysis of the interossei, the diminution of tone in the extensor muscles, and the impairment of synergistic action. There are, in addition, relaxation of the wrist, subluxation of the metacarpophalangeal articulations, and deviation of the hand to the radial side. As further evidence of ulnar paralysis, Leonard directs attention to the "sign of the thumb" in which the second phalanx of the thumb is strongly flexed; but opposition of the thumb to the other fingers and flexion of the first phalanx cannot be performed. The "sign" is attributed to paralysis of the adductor pollicis, and is said to occur more frequently when there is an associated involvement of the median nerve. Atrophy of the interossei is pronounced; the hypothenar eminence is partly atrophic; the little and ring fingers are hyperextended at the metacarpophalangeal joints and cannot be flexed; and, unless the lesion is situated near the wrist, the atrophy involves also the muscles on the ulnar aspect of the forearm.

As a result of this extensive paralysis of the hand, the proximal phalanges are extended; the second and third phalanges are flexed; and abduction and adduction of the fingers are lost. The hand and fingers, accordingly, assume a characteristic position known as "claw-hand," or *main en griffe*. Usually the clawing is most pronounced in the little and ring fingers, but occasionally the middle finger is slightly affected. Recent studies by Pitres and Marchand have shown, however, that the "claw-hand" is not distinctive of ulnar paralysis, since the deformity was noted when there was no lesion of the nerve; and in 10 per cent. of ulnar injuries it failed to develop, although the nerve was completely severed. The clawing may appear immediately after the injury or at a later period, but these immediate and delayed types were found to have no constant relation to the character or gravity of the lesion. In the clawing of the fingers, the distal phalanges may be flexed



in the form of an arc, an open hook, or a closed hook. When the ulnar nerve is injured in the lower part of the forearm or at the wrist, the paralysis is confined to the small muscles of the hand, and the clawing is then especially prominent.

The sensory changes accompanying ulnar lesions are fairly constant and confined to the little and ring fingers on both the dorsal and palmar surfaces, and to the hypothenar eminence. The sensory defect extends as far as the wrist and is particularly marked over the entire little finger where all sense qualities are lost, although the epicritic field is usually more extensive than the protopathic. Excessive local sweating may occur, but vasomotor and trophic changes are uncommon unless there is an associated vascular lesion.

In partial lesions of the nerve, the paralysis is, according to Benisty, often confined to the interossei and hypothenar muscles; but the long flexors are sometimes affected, and clawing may or may not be a feature. Atrophy of the first interosseous space is, however, constantly present. From a study of the dissociated symptoms resulting from incomplete lesions, it is believed that the fibres for the flexors of the fourth and fifth fingers occupy the posterolateral region of the nerve trunk, and those to the flexor carpi ulnaris, the medial portion.

*Diagnosis.*—The atrophy in the first dorsal interosseous space, the abduction of the little finger, the clawing of the hand, and the loss of lateral movements of the fingers are, in Benisty's opinion, sufficient to establish the diagnosis. To these, may be added the "sign of the thumb" and the complete anesthesia of the little finger. Other conditions may, however, closely simulate paralysis of the nerve. Thus, in progressive central muscular atrophy the small muscles of the hand and, particularly those innervated by the ulnar nerve, often exhibit early atrophic changes which result in the development of the typical claw-hand. Sensory disorders are, however, absent and, according to Gowers, the "clawing," in disease of the spinal cord, is not confined to the fourth and fifth fingers; since, owing to paralysis of the two radial lumbricales, the middle and index fingers are also involved. Syringomyelia and cervical rib may likewise affect the ulnar segments; but these are to be recognized by the presence of pain, the dissociated type of sensory loss, and the discovery of an accessory rib in the radiogram. It may also be necessary to distinguish ulnar palsy from traumatic hysteria, injury to the tendons of the long extensors, musculotendinous lesions of the flexors, vascular disorders of the upper extremity, and Dupuytren's contracture.

*Prognosis.*—Recovery is often slow and, after severe lesions, incomplete. According to Benisty, sensory return precedes the recovery of motor function. The muscles regain their innervation in the following order: First, the flexor carpi ulnaris; secondly, the flexor profundus digitorum, by which the clawing of the hand is temporarily increased; and lastly, the interossei, the hypothenar muscles, and the adductor pollicis. Immediate suture of the completely divided nerve does not, according to Galland, insure early recovery; but Haworth has obtained good results from ulnar-median anastomosis; and electricity and massage are useful in maintaining the nutrition of the muscles. Pitres recommends the following test of recovery: Have the patient lay the palm of the hand flat on a table; if he can then move the middle finger in both lateral directions and scratch the top of the table with the little finger without flexing the wrist, recovery is said to be complete.

### THE INTERCOSTAL NERVES

The thoracic nerves, with the exception of the first, second, and twelfth, are distributed to the intercostal, abdominal, and spinal muscles, and convey sensory fibres to the integument of the thorax and abdomen. Intercostal neuralgia and herpes of the trunk are not uncommon; but otherwise, the dorsal nerves are rarely the seat of primary disease, although they may be secondarily involved in tumors of the cord or meninges, and in diseases of the vertebræ, thorax, and abdomen. Sensory disorders of a subjective or objective character, in the distribution of the upper thoracic nerves, are sometimes noted in the course of *tabes dorsalis*; and a primary neuritis of the intercostal nerves has been described.

The lower thoracic nerves to the abdominal muscles are more frequently affected. One or more dorsal segments of the cord are occasionally involved in poliomyelitis; and inflammation of the lower nerve trunks has occurred as a complication of typhoid fever, malaria, gout, diabetes, and alcoholic intoxication. The neuritis may be unilateral or bilateral, with resultant paralysis of the abdominal parietes and the production of pain, paresthesia, numbness, or loss of cutaneous sensibility. The parietic abdominal wall is bulging and relaxed; it does not follow the respiratory movements; and, in the unilateral affection, the umbilicus is deviated to the sound side. With forced inspiration, coughing, crying, and sneezing, protrusion of the abdomen is more pronounced upon the parietic side. The abdominal reflex is lost, and the muscles exhibit the reaction of degeneration. Paralysis of the abdominal wall occurs, occasionally, in the muscular dystrophies; and congenital absence of the individual muscles has been noted.

### THE LUMBAR AND SACRAL PLEXUSES

The sensory and motor innervation of the lower abdomen, the pelvic region, and the lower extremities is derived from the lumbar and sacral nerves which unite in the formation of four plexuses; but ordinarily, only the lumbar and sacral plexuses are of clinical interest. The pudendal plexus, formed from the lower sacral nerves, and its subdivision, the coccygeal plexus, are not often subject to injury or disease, although their fibres may be implicated in lesions of the nerve roots or of the cauda equina.

#### THE LUMBAR PLEXUS (T. 12; L. 1, 2, 3, 4).

Formed, thus, from a portion of the anterior primary division of the twelfth thoracic, the whole of the first three, and larger part of the fourth lumbar nerves, the branches of the plexus are distributed principally to the anterior and internal portions of the lower extremity. Cutaneous branches innervate the lower abdomen, the genital region, the medial, anterior, and lateral aspects of the thigh, and the inner side of the leg and foot. Motor fibres are distributed to the cremaster muscle, the flexors, and the adductors of the thigh, and the extensors of the leg. (Fig. 3.) Primary disease of the lumbar plexus is uncommon, but Mills refers to idiopathic neuritis of the plexus; and lumbo-abdominal neuralgia, probably of neuritic origin, is sometimes associated with neuralgia

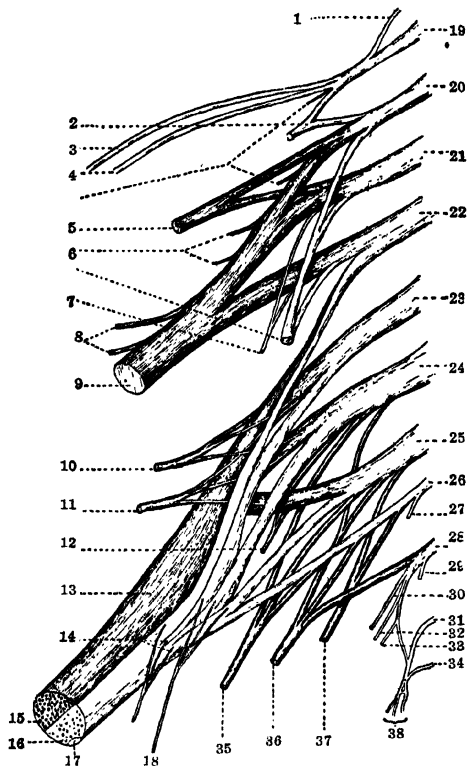


FIG. 3.—LUMBOSACRAL PLEXUS (After Morris).

## 1. From last thoracic nerve

- |                               |                                 |                    |                   |
|-------------------------------|---------------------------------|--------------------|-------------------|
| 2. Genito-femoral             | 19. First lumbar                | } Lumbar plexus    | } Pudendal plexus |
| 3. Ilio-hypogastric           | 20. Second lumbar               |                    |                   |
| 4. Ilio-inguinal              | 21. Third lumbar                |                    |                   |
| 5. Lateral cutaneous          | 22. Fourth lumbar               |                    |                   |
| 6. Obturator                  | 23. Fifth lumbar                | } Sacral plexus    |                   |
| 7. Accessory obturator        | 24. First sacral                |                    |                   |
| 8. To iliacus and psoas major | 25. Second sacral               |                    |                   |
| 9. Femoral (anterior crural)  | 26. Third sacral                |                    |                   |
| 10. To superior gluteal       | 27. Visceral branches           | } Coccygeal plexus |                   |
| 11. To inferior gluteal       | 28. Fourth sacral               |                    |                   |
| 12. To piriformis             | 29. Visceral branches           |                    |                   |
| 13. Sciatic                   | 30. Perineal                    |                    |                   |
| 14. To quadratus femoris      | 31. Fifth sacral                | } Coccygeal plexus |                   |
| 15. Common peroneal section   | 32. To coccygeus                |                    |                   |
| 16. Tibial section            | 33. To levator ani              |                    |                   |
| 17. To hamstrings             | 34. Coccygeal                   |                    |                   |
| 18. To obturator internus     |                                 |                    |                   |
|                               | 35. Posterior femoral cutaneous |                    |                   |
|                               | 36. Pudic                       |                    |                   |
|                               | 37. Perforating cutaneous       |                    |                   |
|                               | 38. Ano-coccygeal               |                    |                   |

of the intercostal nerves. The plexus or its branches may be injured by compression from intra-abdominal tumors, psoas abscess, and aneurysm, or from the fetus during parturition; and disease of the vertebræ, meninges, or spinal cord may, likewise, involve the segments or roots of the lumbar nerves.

#### THE SACRAL PLEXUS (L. 4, 5; S. 1, 2, 3).

Derived largely from the lumbosacral cord, formed by the union of a portion of the fourth, and the entire fifth lumbar roots, the plexus receives fibres also from the first, and a portion of the second and third sacral nerves. The cutaneous nerves are distributed to the skin of the gluteal region, the posterior aspect of the thigh, the lateral and posterior surfaces of the leg, and the greater part of the foot. Its motor branches have to do with extension, abduction, and rotation of the thigh, flexion of the leg, and all the movements of the foot.

Primary disease of the plexus is unusual, but a so-called idiopathic neuritis of most of its branches has been described. Mills is of the opinion that injuries of the lumbosacral plexus are not uncommon and, as a rule, the sacral portion suffers more frequently than the lumbar component. Intra-abdominal disease, ovarian and uterine disorders, and pelvic inflammatory conditions are common sources of damage to the plexus or its branches. Pressure of the fetal head and injury of disease of the sacro-iliac joint may readily implicate the fibres of the lumbosacral cord. Mills has very properly directed attention to the importance of rectal and vaginal palpation as a means of determining the sensitiveness of the sacral and pelvic nerves—a procedure, no doubt, frequently neglected. Occasionally, it may be very difficult to distinguish lesions of the plexus from disease of the spinal cord or cauda equina; and Mills refers especially to the following distinctive features of the plexus lesion: Tenderness of the nerves upon palpation by rectal or vaginal examination, the unilateral distribution of symptoms, the predominance of pain in the sacral area, and the peripheral nerve type or sensory defect. The motor symptoms are usually more pronounced in the muscles below the knee, and vasomotor and trophic disorders are not uncommon. Unless the lowest sacral and pudendal nerves are affected, the sphincters of the bladder and rectum are unimpaired.

**The External Cutaneous Nerve (L. 2, 3).**—The nerve is entirely sensory and, after making its superficial exit at the notch below the anterior superior iliac spine, innervates the skin of the thigh on its anterolateral aspect as far as the knee. Isolated affections of the nerve are uncommon, and are usually characterized by pain, paresthesia, or anesthesia; but, occasionally, they may present some of the features of causalgia. In 1895, Bernhardt described a peculiar affection of the nerve, probably of neuritic origin, which was later designated by Roth as:

**MERALGIA PARESTHETICA.**—Bernhardt's disease or Roth's disease has been defined by Musser and Sailer as "a disturbance of sensation on the external surface of the thigh, characterized by various forms of paresthesia associated with dissociation and more or less diminution of sensation." The disorder is comparatively uncommon, and Musser and Sailer were able to find only 89 cases in the literature; to these they added ten personal observations. Of the total number 75 were in the male. Generally, the condition is unilateral, and the right and left sides are about equally affected. In 20 of the 89 cases, both nerves were in-

volved. The symptoms may occur at any age, but are probably more common within the fourth and fifth decades.

*Etiology.*—The cause of the affection is unknown; but trauma, alcohol, and the infectious diseases are said to be important predisposing factors. The disorder has also been attributed to gout, infectious arthritis, obesity, diabetes, and syphilis. Cold, exposure, and occupation are regarded as contributing factors; and it is thought that the use of hydrotherapy, in the treatment of typhoid fever, is responsible for the occasional appearance of meralgic symptoms during the course of the disease. It is more probable, however, that the affection is, under these circumstances, of toxic origin. Notwithstanding the greater frequency of the disease in the male, pregnancy is said to be an important etiological factor. Paresthetic disturbances in the course of the nerve have been noted also in diseases of the spinal cord and vertebræ, and, more rarely, in conjunction with *tabes dorsalis*.

*Symptomatology.*—The onset of symptoms is often insidious, and initiated by paresthetic disturbances upon the outer side of the thigh. Actual pain is not invariably present; more commonly, there are subjective sensations of burning or heat; and the skin is often acutely hypersensitive to light touch. At first, these symptoms may be experienced only when there is unusual tension upon the fascia lata from prolonged standing or walking. Relief is generally obtained after a variable period of rest; but, in some instances the discomfort is greatest when the patient is in bed and, occasionally, there are nocturnal exacerbations. Rarely is there tenderness upon pressure over the nerve trunk at the superior iliac notch; but the skin of the affected region may be smooth and hyperemic, or rough and tense, and the surface temperature is sometimes elevated. Gross trophic changes have, however, not been noted. Objectively, there is often an unequal or dissociated sensory defect in which pain and electrocutaneous sensibility are chiefly affected. Liebers finds, in the beginning, a loss of both epieritic and protopathic sensibility, and occasionally, a condition of hyperalgesia. Sometimes, the paresthesia extends into the femoral area on the anterior and medial surfaces of the thigh; and, not infrequently, diminished sensibility to the faradic current may be detected in the external cutaneous area of the opposite thigh, although the patient was previously unaware of any sensory defect in the region.

The course of the disease is often protracted and may extend over a period of years, during which the symptoms alternate with variable intervals of complete relief. The frequency with which the affection is associated with fatigue, overwork, prolonged standing or walking, and the occasional relief obtained after a period of rest, present a close analogy to the symptoms of intermittent claudication; but the vascular disturbances, muscle cramps, and more frequent occurrence of pain in the latter affection serve to differentiate the two diseases.

*Treatment.*—The treatment of meralgia is generally unsatisfactory. **Rest in bed** is recommended, and, in the so-called rheumatic cases, the **salicylates** are said to be of some use. Counterirritation usually aggravates the condition, but much relief is sometimes obtained from careful **faradization of the cutaneous area**. Massage is of questionable value. In some instances, stretching or resection of the nerve has been practiced with good results, and it occurs to the author that the injection of alcohol into the nerve trunk, at the iliac notch, may be equally efficacious.

**Pathology.**—The nature of the lesion is not known, but it is believed that the affection is of neuralgic or neuritic origin. Nevertheless, the pain is not of the neuralgic type; and objective sensory defects form no part of a true neuralgia. On the other hand, the occasional absence of pain, the frequent failure to elicit nerve tenderness, and the total lack of trophic changes appear to discredit the neuritic character of the disease. Histological examination of the resected nerve has, thus far, shown no constant pathological condition. Bramwell, and Souques found no evidence of inflammation or degeneration, but Narwratzki has recorded an instance in which there were evidences of a perineuritis and myelin degeneration.

**The Obturator Nerve (L. 1, 2, 3, 4).**—The nerve contains both sensory and motor fibres and occupies a protected position behind the psoas muscle. Motor fibres are distributed to the adductor longus, adductor brevis, adductor magnus, obturator externus, and gracilis muscles and, at times, to the pectineus. Sensory filaments innervate the hip and knee joints, and the medial surface of the thigh in its upper third; but the branch to the knee joint is sometimes absent; and, occasionally, the cutaneous innervation extends as far as the inner side of the knee.

Paralysis confined to the obturator nerve is unusual, but it has been observed, in obstetrical practice, as the result of prolonged or instrumental delivery, and from the pressure of pelvic tumor and obturator hernia. The symptoms are manifested by inability to fully adduct the thigh or rotate it externally, and the legs cannot be crossed without assistance. The muscles on the inner part of the thigh are flaccid, and later show the reaction of degeneration. Objective sensory changes are not ordinarily present, but irritative lesions of the nerve may be the cause of pain which is referred to the hip or knee joints; and, occasionally, in disease of the hip joint, irritation of the obturator fibres has been productive of pain which is localized entirely in the knee.

**The Femoral or Anterior Crural Nerve (L. 1, 2, 3, 4).**—This, the largest branch of the lumbar plexus, is formed by the union of the first four lumbar nerves within the substance of the psoas muscle. The nerve trunk then occupies the groove between the iliacus and psoas, and leaves the abdominal cavity behind the ligamentum inguinale to enter the thigh at the outer side of the femoral vessels. Motor fibres are furnished to the iliacus, sartorius, pectineus, and quadriceps femoris muscles. Cutaneous branches are distributed to the anterior and medial surfaces of the thigh, and the inner side of the leg, foot, and great toe. Sensory filaments are also supplied to the hip, knee, and ankle joints. The internal saphenous, its longest branch, is entirely sensory.

**PARALYSIS OF THE NERVE.**—Direct injury of the nerve trunk from external violence is unusual, but its fibres are not infrequently implicated in tumors of the cauda equina, and in diseases of the meninges and vertebrae. Psoas abscess, intra-abdominal tumors, and inflammation may also be the cause of femoral paralysis; and the nerve is sometimes involved in diseases of the femoral triangle, dislocation of the hip, and inflammation about the knee joint.

The symptoms resulting from paralysis of the femoral nerve vary according to the situation of the lesion. When the nerve is injured within the pelvic cavity the fibres to the psoas muscle usually escape, so that flexion of the thigh on the abdomen is not greatly impaired; but there is total paralysis of the quadriceps extensor muscle, and consequent inability to extend the leg. The muscles on the anterior portion of the

thigh are atrophic and exhibit the reaction of degeneration; the knee-jerk is abolished; the gait is defective; and, because of relaxation of the knee joint, there is especial difficulty in ascending a stairway. Sensory loss is noted on the entire anterior and most of the medial surfaces of the thigh, and the inner side of the leg and heel. Lesions of the nerve within the thigh result in a more restricted muscle involvement, although the sensory defect extends throughout most of the internal saphenous area. In partial and irritative injuries, the motor paralysis is not so wide-spread, and pain, paresthesia, and nerve tenderness may be added features. Gowers describes an obscure, sensory affection of the nerve occurring in the aged, in which the symptoms are largely subjective and confined to the lower half of the anterior surface of the thigh. The muscles are not affected.

**NEURITIS OF THE FEMORAL NERVE.**—Inflammation of the femoral nerve may occur as part of a plexus neuritis or a multiple neuritis, but a femoral mononeuritis is said to be of infrequent occurrence. In a previous study, the author has, however, collected from the literature one hundred and thirty-six instances in which the femoral nerve alone has been the seat of disease. Eleven of the cases were bilateral. The affection occurred eighty-four times as a postpartum complication of toxic origin, eight times as an idiopathic disorder, and once as a congenital paralysis. Gout, diabetes, appendicitis, typhoid fever, ether narcosis, occupation, and exposure were said to be of etiological importance in the remaining cases.

The affection is more common in the fifth and sixth decades and, with the exception of the obstetrical cases, is about three times more frequent in men than in women. The symptoms are manifested by pain and tenderness along the course of the nerve, paresthesia or hypæsthesia, and weakness or paralysis of the extensor muscles. Vasomotor and trophic disturbances are sometimes observed, but anesthesia is uncommon. Usually, the pain is continuous, deeply seated within the bones or joints, and characterized by nocturnal exacerbations. Very often, the patient indicates the seat of pain in the distinctive manner already related in the description of neuritis in general.

Ordinarily the diagnosis is not difficult. The so-called idiopathic affection may simulate, very closely, disease of the spinal cord; but the nerve tenderness, the type of motor paralysis, the absence of sensory loss, the character of the pain and the manner in which its course is delineated are helpful differentiating features. Treatment is directed according to the etiology, the specific requirements of the local condition, and the principles recommended in the treatment of neuritis in general.

**The Superior Gluteal Nerve (L. 4, 5; S. 1, 2).**—The nerve trunk arises from the posterior aspect of the lumbosacral cord, and is composed entirely of motor fibres for the innervation of the gluteus medius, the gluteus minimus, and the tensor fasciæ latæ. The gluteus medius has to do with abduction and rotation of the thigh. The anterior portion of the muscle produces internal rotation; contraction of the posterior fasciculi results in external rotation of the thigh; and when the entire muscle contracts the movement is one of abduction and slight internal rotation. The gluteus minimus abducts and rotates the femur inward, and when it acts in conjunction with the medius there is a moderate degree of circumduction.

Isolated paralysis of the gluteal nerve is rarely observed, although it has been noted in pelvic and vertebral disease, and during parturition.

More commonly, the nerve is involved along with the sciatic or the lumbo-sacral cord. As a result of its paralysis, the thigh cannot be abducted; circumduction is defective; and the femur is rotated slightly outward.

Paralysis of the inferior gluteal nerve, which innervates the gluteus maximus, causes marked weakness in extension of the hip and consequent difficulty in the act of ascension. The paralyzed muscle is atrophic; the gluteal region is flattened; and the electrical reaction is of the degenerative type.

**The Sciatic Nerve (L. 4, 5; S. 1, 2, 3, 4).**—This, the largest nerve in the body, consists of two distinct parts united into a common trunk as far as the upper portion of the popliteal space. Here the common peroneal (external popliteal) and tibial (internal popliteal) nerves acquire a separate sheath, although in about 10 per cent. of the cases the two trunks remain distinct throughout their entire course. The main trunk of the sciatic nerve contains sensory, motor, vasomotor, and trophic fibres. Motor nerves are distributed to the muscles on the posterior aspect of the thigh and to all of the muscles of the leg and foot. Through its sensory branches, cutaneous filaments innervate the skin of the inferior gluteal region, the back of the thigh, the postero-external portion of the leg, and dorsolateral part of the foot. In its passage through the thigh, the nerve is accompanied by a nutrient artery which, according to Compton, is situated between the two main divisions of the trunk as far as the inferior border of the gluteus maximus muscle.

In an effort to determine its particular pattern, its reaction to injury, and its method of recovery, the internal structure of the sciatic nerve was, during the recent war, a subject of special investigation. Compton finds that, although its two main divisions are not always distinct, the fibres of the peroneal nerve generally occupy a position to the outer side and somewhat anterior to the tibial fasciculi; that the posterior portion of the tibial and peroneal nerves are composed largely of sensory fibres; and that the tibial branch possesses a more vascular connective tissue sheath. It was also observed that the two divisions do not, as a rule, leave the trunk at a constant level; hence, it was quite impossible to recognize them from their point of departure. McKinley's study of the nerve in man and after experimental section in dogs, failed to reveal any evidence of segmental grouping of fibres in the main trunk, but indicated that the two branches form, throughout most of their course, an intricate plexus of fibres, which renders it especially difficult to establish a fixed "nerve pattern." The motor fibres to the biceps femoris, the semitendinosus, and the semimembranosus muscles of the thigh leave the main trunk at the level of the gluteal fold; consequently, the paralytic symptoms, resulting from injury to the nerve, vary when the lesion is situated above or below the origin of these muscular branches. The character of the paralysis also depends upon whether the nerve trunk has been partially or completely divided.

**PARALYSIS OF THE NERVE.**—Although the nerve rarely escapes in wounds of the posterior part of the thigh, lesions in this situation are comparatively uncommon in civil life. More often, the damage is due to diseases of the pelvis, fracture or dislocation of the hip, and inflammation of the bones or soft parts. Neuroma of the trunk is said to be not uncommon; and the nerve is, according to Gowers, prone to inflammatory affections. Benisty found military injuries of the sciatic nerve almost as frequent as those of the radial, although the lesion was more



often partial, and the resulting paralysis, therefore, not so disabling as that following a complete destruction of the femoral nerve.

*Symptomatology.*—When the nerve is totally divided near the sciatic notch there are resultant paralysis of the posterior muscles of the thigh, all the muscles of the leg and foot, and loss of sensation throughout the sciatic distribution. More often, however, the nerve is injured in the lower two-thirds of the thigh, and in this situation the hamstring muscles escape. Thus, paralysis of the leg and posterior muscles of the thigh is indicative of a lesion of the sciatic near its radicular origin within the plexus, or in the cauda equina. Following the injury, the foot is dropped and inverted; the plantar arch is slightly flattened; the toes are flexed; and, when the hamstring muscles are involved, movement of the leg is impossible. The paralysis may be readily demonstrated by the patient's inability to move the foot or leg when the knee is extended. It is still possible, however, for him to walk, since the flexors of the hip in the anterior femoral group, enable the entire lower extremity to be moved in a forward direction.

Subjective sensory disturbances are not particularly prominent, but occasionally, there is a sensation of pain, coldness, or swelling in the leg, which may seem as if it were a detached part. Vasomotor and trophic changes are not of great importance; nevertheless, the skin on the dorsum and outer side of the foot, is, at times, cyanotic, dry, or scaly, with slight elevation of the surface temperature. Perforating ulcer has been noted. Because of the vasomotor changes and the consequent edema there is, at first, little evidence of muscular atrophy, although the reaction of degeneration may be complete. Objectively, cutaneous sensibility is lost on the outer and posterior portions of the leg, the larger part of the dorsum of the foot, and the entire plantar surface. If the small sciatic has also suffered, the sensory loss is more extensive, and involves the inferior gluteal region and the posterior aspect of the thigh. Postural sense and the vibration sense are often defective. The Achilles jerk is abolished. Unless there is definite inflammation, the nerve trunk is not tender to pressure; but partial lesions of the nerve are often painful, particularly when the tibial fibres are implicated, and causalgia is, then, not an infrequent symptom.

Recovery is usually initiated by tingling or painful sensations, and by twitching of the muscles when the nerve is compressed; and these may precede, for an appreciable period, the return of voluntary motion. Objectively, recession of the anesthetic field occurs only a short time before the restoration of motor function, which often appears abruptly and, according to Benisty, in the following order: First, in the tibialis anticus or in the peronei, and lastly, in the long extensors of the toes. It may be many months before perfect function is regained; but recovery is always more prompt and more nearly complete, the nearer the lesion to the popliteal space, since in this situation, disarrangement of the nerve pattern is not so likely to occur. Pitres states that when the patient can alternately raise the body on the heel and toes, or beat "common time" with the injured foot, recovery may be regarded as complete.

**The Tibial or Internal Popliteal Nerve (L. 4, 5; S. 1, 2, 3, 4).**—Arising from the last two lumbar and first three sacral roots, the nerve passes vertically through the popliteal space and descends into the leg, where it divides, at the ankle, into the lateral and the medial plantar nerves. Sensory fibres are distributed, through the short or external

saphenous branch, to the lower third of the leg on its posterior surface, and to the heel and external part of the foot. Articular filaments are conveyed to the knee and ankle joints, and motor branches innervate the popliteus, the calf muscles, the tibialis posticus, the long flexors of the toes, and the intrinsic plantar muscles. The studies of Marie, Meige, and Gosset indicate that the internal structure of the nerve conforms to the following pattern: The fibres to the flexors of the toes occupy the postero-internal region of the nerve trunk; those to the gastrocnemius and soleus are situated in its posterior portion, while the tibialis posticus is represented on its antero-internal surface.

**PARALYSIS OF THE NERVE.**—Direct injury to the nerve in the popliteal space, or in the tibial portion of the sciatic is relatively uncommon. During the World War, Benisty failed to find a single instance in which the nerve, alone, was completely severed; but partial or dissociated lesions were of frequent occurrence, and very often associated with involvement of the external popliteal. Tumors and inflammatory diseases at the knee may be the cause of tibial paralysis, and McArthur has observed a primary sarcoma of the nerve trunk.

The symptoms resulting from complete division of the nerve are readily recognized by the anatomical distribution of the sensory and motor defects; but most lesions are of the dissociated types and present a more complex syndrome in which pain is often a constant feature. According to Benisty, causalgic attacks in the calf, or outer side of the foot are not infrequent. The leg and foot may be edematous, and the skin dry, scaly, or cyanotic; but trophic changes are particularly uncommon. Objectively, there is loss of cutaneous sensibility on the lower posterior part of the leg, the outer portion of the sole, and the plantar surface of the toes. The motor paralysis is characterized by inability to extend the foot, the development of talipes calcaneus, and flexion of the digits at their distal phalanges, with the production of "hammer-toes." Walking is, therefore, greatly impaired. The Achilles tendon is atonic and less prominent than on the sound side; the ankle-jerk is abolished; and the parietic muscles exhibit the reaction of degeneration with subsequent atrophy.

**The Common Peroneal or External Popliteal Nerve (L. 4, 5; S. 1, 2, 3).**—After separating from the main trunk of the great sciatic, the peroneal nerve descends along the outer margin of the popliteal space and turns forward at the neck of the fibula to enter the leg, where it divides into recurrent articular, superficial peroneal (musculo-cutaneous), and deep peroneal (anterior tibial), branches. Sensory nerves innervate the integument on the lateral and anterior portion of the leg and the dorsum of the foot. Articular filaments are furnished to the ankle and foot. Motor fibres are distributed to the tibialis anticus, the extensor longus digitorum, the extensor brevis digitorum, and the peroneal muscles. The fibres for the long extensor of the toes are situated in the antero-external portion of the trunk, and those for the tibialis anticus on its antero-internal surface, while the external surface of the nerve contains the fibres for the extensor proprius hallucis. On the posterior surface are the axones to the peroneus longus and the peroneus brevis. In its anatomical disposition, its physiological function, and its diseases, the common peroneal nerve is said to be analogous to the radial.

**PARALYSIS OF THE NERVE.**—Isolated paralysis of the nerve is not uncommon. Its superficial position, as it enters the leg, exposes it to

various forms of external pressure, and injury from fracture or dislocation at the knee joint. Generally, the lesion is complete, and is followed by immediate paralysis. Mononeuritis of the peroneal nerve is of infrequent occurrence.

The symptoms are comparable to those of radial palsy. Thus, the foot occupies a position of "foot-drop;" it cannot be flexed dorsally; and there is consequent development of the characteristic steppage gait. At the same time, the foot is slightly inverted; the first phalanx of each toe is dependent; and the tarsal bones are more prominent. True eversion of the foot cannot be performed, and the extensor tendons at the ankle are no so prominent as on the sound side. Muscular atrophy and the reaction of degeneration are present in long-standing paralysis. Paresthetic, vasomotor, and trophic changes are not specially prominent, but objective loss of sensation in the distribution of the superficial peroneal branch is constantly present. Retraction of the anesthetic field and return of motor function occur almost simultaneously.

**The Plantar Nerves.**—Occasionally, the medial and lateral plantar nerves are subject to a painful disorder usually attributed to a local neuritis or neuralgia. The affection is thought to be the result of certain occupations which necessitate prolonged standing or walking, and the symptoms are mostly subjective; but anesthesia and motor paralysis have been noted. Incised wounds of the foot may implicate either one or both plantar nerves; and because of the resulting flexion and contracture of the toe, injuries of the external plantar nerve are more disabling than when the lesion is confined to the inner branch alone.

## THE SCIATICAS

**Definition.**—Sciatica has been defined as a painful inflammatory disease of the sciatic nerve, and until within the past decade, has occupied a prominent position as a clinical entity. It is also designated as ischias, ischialgia, neuralgia femoro-poplitea, and malum cormunni in recognition of the pioneer studies of Cotugno. This varied nomenclature is, in itself, a confession of uncertainty concerning the origin and nature of the affection; and later refinements in diagnosis seem to indicate that sciatica is nothing more than a clinical syndrome, possessing either the feature of a neuralgia or a neuritis, dependent upon a number of etiologic factors. Nevertheless, there still remains a small group of ischialgias of unknown origin for which is reserved the term "sciatica." Thus, a primary and a secondary type were recognized by Buzzard and Gowers; and although modern methods of investigation have not eliminated the so-called idiopathic affection, the physician who is content with a diagnosis of sciatica is courting therapeutic disaster, since the labelling of the syndrome in this fashion is, in Nutter's opinion, only an effort to give a name to a large group of painful disorders of the sciatic nerve. McCrae is of the belief that "sciatica" is no better diagnosis than "headache," and Ely suggests that "sciatica," "belly-ache," and "acute bilious attacks" be thrown into a common waste-basket.

Because of the ephemeral character of the symptoms and the absence of neuritic features in some cases, it has been assumed that clinically, at least, there is a type of sciatic neuralgia; but sciatica means inflammation of the nerve and does not, therefore, properly designate a true

neuralgia; hence, "ischialgia" is accordingly suggested as a more distinctive name for the true neuralgic affection. Regardless of the etiology or supposed idiopathic origin, "sciatica" should then be reserved for that form of the affection in which there are clinical evidences of a true neuritis.

**Types of Ischialgia.**—Painful affections of the sciatic nerve are, in the majority of cases, symptomatic; and Rosenheck and Finkelstein have divided the affection into three types: A symptomatic sciatica, an orthopedic sciatica, and a neuritic sciatica. Sicard and Roussay prefer, however, an anatomical classification in which three groups are recognized: First, a low type affecting the nerve at the popliteal space; second, a more common middle type confined principally to the femoral portion of the nerve; and lastly, a high type, or radiculitis, involving the nerve roots between the vertebræ and the plexus. Leszynsky describes a perineuritic, a radiculitic, a neuritic, and a neuralgic form; and, to these, Strauss adds a lumbosacral type of the disorder.

**Incidence.**—As a symptomatic affection, ischialgia is, in Solomonson's opinion, the most frequent type of nerve pain, but he regards the primary or idiopathic form as particularly rare and of questionable occurrence. The disorder is most common from the third to the fourth decade, and is said to be unknown in childhood, although it has been observed as early as the fifteenth year. The frequency with which the disease affects the two sexes appears to vary slightly in different clinics. Solomonson finds 78 per cent. of the cases in the male, but Strauss is of the opinion that the male and the female are about equally affected. There is slight predominance of the left-sided disease and, according to Gowers and Solomonson, the condition is bilateral in about 7 per cent. of the cases. It is generally believed that sciatica is more common in the spring and summer months.

**Etiology.**—Heredity is said to take no part in the cause of the disorder, but those who look upon the condition as a primary clinical entity attach much importance to the gouty and rheumatic affections; and exposure is thought to be particularly predisposing. More accurate methods of investigation have, however, disclosed a great many etiological factors which had previously been overlooked; so that the existence of a primary idiopathic sciatica is regarded with increasing unpopularity.

Injuries to the sciatic nerve are not, in the strictest sense, included among the etiological conditions, although symptomatic sciatica is not infrequently the result of pressure from intra-pelvic tumors, the gravid uterus or the blade of the forceps during instrumental delivery. Violent muscular exertion, faulty posture of the leg during surgical operations in the prolonged lithotomy position, an awkward manner of sitting with the legs crossed or compressed by the edge of the chair, overexertion, and the continued use of the sewing-machine have been responsible for the development of minor sciatic disorders. The pressure of fecal impaction has been mentioned as a cause of left-sided sciatic pain. Psoas abscess, and direct injury to the nerve from the injection of medicated substances into the buttock are occasional etiological factors; and excessive adiposity, with resulting pendulous or prominent abdomen, may, according to Nutter, exert undue tension upon the lumbar spine, and thus produce a type of sciatic radiculitis. In some instances flat-foot is thought to be an exciting cause.

Acute and chronic pelvic inflammatory disease in the female, and specific or nonspecific prostatitis and epididymitis in the male have, either directly or by extension of the inflammation, implicated the fibres of the sciatic nerve. Osteomyelitis, bony tumors, a sudden strain, fracture, dislocation, malformations of the pelvis, arthritis of the lumbosacral, the sacro-iliac, and, more rarely, the hip joints are additional causes of sciatica. In fact many orthopedists and, not a few internists, are of the opinion that the majority of the sciaticas are due to disease of the pelvic articulations or synchondroses; and evidence of the correctness of this view is constantly accumulating. Rogers, from a study of the records at the Massachusetts General Hospital, finds that fifteen years ago almost all of the cases of sciatic pain were admitted first to the Neurological Department; while, more recently, these patients have been referred direct to the Orthopedic Clinic, so that during the latter part of 1917 only 3 cases of sciatica were admitted to the Neurological Service. Although it is the custom at the Johns Hopkins Hospital Dispensary to admit this class of patients to the Neurological Department, the author has not, within the past ten years, observed a single instance in which a transfer was not subsequently made to the Orthopedic, or some other department, for further study or treatment; and, as a rule, some bony, articular, or medical disorder was found to be responsible for the nerve symptoms.

The constitutional and infectious diseases are occasionally productive of isolated inflammation of the sciatic nerve or, more frequently, the sciatica is part of a plexus or multiple neuritis. A diabetic sciatica, in which one or both nerves may be affected, is not uncommon. The bilateral form is, however, more often observed, and the extent of the lesion is said to be proportionate to the sugar output and the degree of acidosis. Grave anemias and the cachexia of malignant disease are occasionally the cause of sciatic neuritis. Of the infectious diseases, influenza plays a prominent part, and the nerve has also been affected in pneumonia, scarlet fever, typhoid fever, malaria, tuberculosis, and puerperal fever. Syphilis as a cause of sciatica was described as early as 1740 by Astruc and, later, by Cerillo, in 1803. Since then it has been recognized by Trousseau, Fournier, and particularly by Déjerine in his studies upon radiculitis. Boudet, in a study of 150 cases of medical sciatica, found the blood Wassermann positive in 38.6 per cent. The spinal fluid examination was of less diagnostic value, and in only one instance was the Argyll-Robertson pupil demonstrated. He is of the opinion that syphilis is a not infrequent etiological factor, and Solomonson's statistics tend to confirm this view. The clinical features in the syphilitic affection are, according to Boudet, distinguished by the more frequent nocturnal exacerbations, the presence of tenderness at the anterior superior iliac spine and in the femoral area, the more constant intensification of the pain upon coughing, and the greater degree of sensory defect. In three instances herpes was a complicating feature. Antileptic therapy was, in most cases, followed by complete relief.

Occasionally, an isolated sciatic neuritis has been attributed to poisoning from alcohol, lead, arsenic, mercury, and carbon monoxid. Reinhardt attaches much etiological importance to varicosities upon the nerve trunk, and Leszynsky, upon one occasion, found the symptoms due to a neurofibroma of the sciatic nerve.

**Symptomatology.**—Pain, the characteristic feature, is, in the beginning, of periodic occurrence with gradations of intensity, but later becomes more or less continuous. An acute type of the affection with slight rise of temperature and general malaise has been described, and Galtier has observed constitutional and vascular changes in a number of instances. He finds also general depression, fatigue, arterial hypertension, tortuosity of the temporal arteries, restlessness, insomnia, and even hallucinations as associated symptoms. During the earlier stages, the pain is sometimes continuous, with occasional sharp, shooting, neuralgic attacks, or it may be diffuse, deeply seated, and radiate from the hip downward or in the opposite direction. Nocturnal exacerbations are common. At times, the pain is atypical and located more particularly in the buttocks or on the inner side of the thigh; but, rarely, is it so strictly limited to the nerve trunk as in the genuine neuralgic affection. Movement of the extremity increases the suffering, and nerve tenderness is a frequent symptom. As the disease becomes more protracted, the pain acquires more of an intermittent and neuralgic character, and is often localized about the lumbosacral and sacro-iliac regions. In typical cases the patient outlines fairly accurately, with the tips of the fingers, the general course of the sciatic nerve.

Very often, there are certain areas about the trunk and lower extremity, known as Valleix's points, which are the seat of spontaneous pain or are especially tender upon palpation. Thus, it is not uncommon to find an acutely sensitive spot over one or more of the following regions: the posterior superior iliac spine, the middle of the iliac crest, the sciatic notch, the great trochanter of the femur, and the external malleolus. The nerve trunk is often tender to palpation in the middle of the posterior aspect of the thigh, in the popliteal space, and over the head of the fibula. Occasionally, the dorsolateral surface of the foot is acutely hypersensitive, but the outer side of the leg and sole of the foot are, as a rule, not particularly painful. At times, the tip of the fifth lumbar vertebra is particularly sensitive, and muscle tenderness is commonly present. Objective loss of sensation is, however, unusual, but paresthesia and hyperesthesia are often annoying, and the temperature sense may be slightly diminished.

The attitude and gait are distinctive and designed to avoid tension upon the nerve trunk. All movements are cautiously performed, and the patient sits with most of the weight upon the unaffected buttock. When standing, there is slight elevation of the pelvis on the painful side; the hip and knee are slightly flexed; the foot is extended; and, in prolonged cases, a moderate degree of contracture may develop with partial fixation of the extremity in this position. This protective attitude is manifested in the gait, which is slightly limping, with the body bent forward, and the heel lifted from the ground so that most of the weight rests upon the ball of the foot.

Motor paralysis with atrophy of the muscles is rarely observed, although in chronic cases a moderate degree of atony, fibrillary twitching, and the reaction of degeneration have been noted, and contracture or spasm of the muscles about the hip and lumbar regions are occasionally present.

Scoliosis is often an associated symptom. The curvature may be homologous or heterologous, with compensatory scoliosis of the thoracic spine, and, in the bilateral affection, lumbar kyphosis is sometimes ob-

served. The homologous scoliosis is said to disappear when the patient is in the reclining posture.

As a rule, the skin reflexes are unchanged. When the affection is confined to the sciatic nerve, the knee-jerk is active and of normal intensity; but atypical cases have occurred in which the knee-kick on the affected side and, occasionally, on the opposite side is diminished or lost. The tendo-Achillis reflex is sometimes retained or even exaggerated, but more often it is diminished or lost; Strauss found it abolished in 10 per cent. of 91 cases. The gluteal reflex, which is obtained by percussing the attachment of the gluteus maximus over the second, third, and fourth sacral bones, is in the opinion of Vidoni, often exaggerated; and, according to Rose, it is occasionally bilaterally increased, although it may be abolished on the affected side. Barré has observed loss or diminution of the retromalleolar reflex, and Buscanio refers to abolition or inversion of the oculo-cardiac reflex, inequality of the pupils, and tachycardia; Giordano, however, finds these sympathetic disturbances of little diagnostic value.

Vasomotor and trophic changes are unusual, but the skin is, at times, moist, dry, or scaly; and discoloration, erythema, acne, herpes, and perforating ulcer have been described.

**SPECIAL METHODS OF EXAMINATION.**—The earlier literature of sciatica is, it seems, overburdened with the description of a variety of "signs" and "tests," which are thought to distinguish the so-called clinical entity, or primary sciatica, from the many secondary and analogous painful affections of the sciatic nerve. It has also been the custom, in many instances, to designate the test by the name of its discoverer, and it may be well to retain this method of presentation for those signs with which the reader is more or less familiar.

*Lasègue's Sign.*—The object of the test is to make tension upon the sciatic nerve and, thus, demonstrate the hypersensitiveness of the nerve trunk by the increased painful reaction. Ordinarily, the test is performed by flexing the thigh on the abdomen with the leg flexed at the knee. In sciatica, this movement is not painful and, therefore, serves to distinguish the nerve affection from disease of the hip joint; but if the leg be passively extended, pain is experienced along the course of the nerve, so that the movement is inhibited before complete extension of the leg is secured. It is necessary, however, to distinguish the pain produced by tension on the nerve from that which also occurs even on the healthy side, due to traction upon the ham-string muscles.

A similar reaction may be obtained by having the patient, with the knees extended, attempt to touch the floor with the hands. It will, then, be observed that the knee on the affected side is flexed; the heel is slightly elevated; and the body is partly rotated to the painful side. Rogers is of the opinion that the pain induced by this movement is not due to tension upon the nerve, but to strain or pull upon the sacro-iliac joint, since he finds it equally painful to make passive hyperextension of the thigh when the patient is lying upon the abdomen. This latter procedure obviously does not exert tension upon the sciatic nerve, and may, therefore, be of some value in discriminating between the arthritic and the so-called primary neurogenic type of sciatica.

A third method of performing the Lasègue test is to have the patient, while sitting on a chair, attempt to extend the legs; this effort increases

the pain in the affected leg, and thus prevents its complete extension at the knee.

Although the sign may be positive, when performed by any of the three methods, it is not distinctive of sciatic affection, since the neurotic patient very often reacts to the test in a similar fashion. Giordano is of the opinion, however, that the malingerer may be detected by the production of pain when the thigh is hyperextended; but it is essential, under these conditions, to exclude disease of the bones or joints. Carhill has observed that a positive Lasègue sign is sometimes accompanied by dilatation of the pupil, a rise of blood-pressure, and tachycardia; and it is his belief that, when these associated features are present, they serve to distinguish the true sciaticas from those of psychogenic origin.

*Kernig's Sign.*—This is not infrequently confused with the preceding sign, and, like it, is only another means of exerting tension upon the nerve trunk. With the normal individual in the dorsal decubitus, both legs can be fully extended; but when Kernig's test is positive, one or both knees are partly flexed and cannot be actively or passively extended. The sign was first observed as a symptom in meningitis, and originally described as an inability to assume the sitting posture in bed without flexing the knees. If the sciatic patient attempts to assume this posture, the affected leg is flexed at the knee, and the pain is intensified when the movement is inhibited. The test may also be elicited by having the patient sit on the floor with the legs outstretched. The leg on the affected side is then incompletely extended, and if an effort is made to depress the knee, pain is produced along the course of nerve. Gowers described the following method of making tension upon the nerve: The patient is seated on a chair and the body slightly flexed on the pelvis; firm pressure is then exerted in the popliteal space which subjects the sciatic nerve to a certain degree of hypertension, with resulting intensification of the pain.

*Patrick's Sign.*—As a means of distinguishing sciatica from hip-joint disease, Patrick describes the following manoeuvre: With the patient lying on the back, the heel of the painful extremity is placed upon the opposite knee; the leg is, accordingly, flexed, the knee elevated, and the thigh partly flexed, abducted, and rotated externally. When the normal individual, or the sciatic patient, assumes this posture the knee is only slightly elevated and may be passively depressed almost to the level of the bed, without producing pain or rotation of the pelvis; but, if there is disease of the hip-joint, the knee occupies a more elevated position and cannot be depressed, without accompanying pain and active inhibition. It is necessary, however, in making the test to avoid deception by wilful tilting of the pelvis; and the test is, according to Patrick, never painful in genuine sciatic neuritis. Leszynsky finds the procedure of diagnostic value, and the author has repeatedly used it as a means of detecting the sacro-iliac type of sciatica, in which it is very often productive of pain in the joint and, to a small extent, along the course of the nerve.

The scoliosis and the homolateral elevation of the pelvis are sometimes designated as Charcot's sign, but the indiscriminate use of proper names for the designation of clinical phenomena is often confusing; and in this connection, it will be recalled that Charcot's name has also been attached to a number of disease manifestations in widely separated conditions. The pain occasioned by forcible and excessive adduction of



the thigh is known as the sign of Bonnet; and tenderness of the adductor muscles is, according to Barré, a common feature of the disease. The French school, and Déjerine in particular, has taught that the increased pain produced by coughing, sneezing, and forced respiratory movements furnishes a means of distinguishing lumbosacral radiculitis from sciatic affections; but Giordano, Barré, and others have found the test equally painful in diseases of the nerve trunk.

Obliteration of the gluteal fold is often regarded as an indication of disease of the sciatic nerve, although its diagnostic value in sciatica is discredited because of its occurrence in atony of the gluteal and posterior thigh muscles from causes other than isolated sciatic affections. Carlill has noted, however, that the fold is often obliterated when there is no atony or flexion of the thigh; and it is his opinion that the sign is, therefore, of clinical value in diseases of the sciatic nerve. It is said to be almost invariably associated with loss of the knee-jerk.

As a result of the flattening and broadening of the Achilles tendon, consequent upon the hypotonia of the calf muscles, Rimbaud has described obliteration of the retromalleolar depression on each side of the tendo calcaneus. He finds the sign present in 75 per cent. of traumatic diseases of the nerve, and in 25 per cent. of genuine medical sciaticas. Rimbaud has directed attention also to a "dissociated muscle response," as evidence of sciatic involvement. It was found that percussion of the plantar surface in the normal individual produces three types of reaction: Thus, if the middle portion be percussed, there is resulting flexion of all the toes; when the stimulus is applied to the internal portion, the response is confined to abduction and flexion of the great toe; while irritation of the lateral aspect, causes a reaction confined largely to the little toe. It was noted, in sciatica, that the response obtained from the center of the sole is the first to disappear, and that it may be abolished sometime before there is diminution or loss of the Achilles jerk; when the nerve is completely sectioned, this central type of reaction is immediately lost, although the response obtained from the inner plantar surface may persist for several weeks.

*The Sign of the Great Toe.*—This is described by Villaret, Faure, and Beaulieu and is said to be of considerable diagnostic value. A study was made of traumatic and medical diseases of the sciatic nerve, and it was observed that percussion of the tendo-Achillis not infrequently caused flexion of the great toe at its terminal phalanx only. The response, thus, differs from the flexion of both phalanges normally obtained upon plantar or submalleolar irritation. Usually, the reflex is more readily elicited by percussing the outer border of the tendon while the patient is kneeling in a chair, or lying upon the abdomen with the legs flexed; and the clinical importance of the sign has since been acknowledged in the writings of Boveri, Fromental and Aulagnier.

*The Sensory Achilles Sign.*—This is said to be helpful in differentiating the true from the false sciaticas. D'Allonnes found, in a study of 110 cases of sciatic lesions that, when the nerve is completely severed, the tendo-Achillis is insensitive to pinching. In disease of the peroneal nerve the sensitiveness of the tendon is only slightly diminished, while lesions of the tibial nerve cause a more pronounced sensory defect. Complete anesthesia of the tendon occurs only when the sciatic trunk is affected; and in polyneuritis, sensation is lost in the tendon on both

sides. During regeneration, there is a period of acute hypersensitiveness, before the normal sensibility of the tendon is restored.

Finally, Neri claims to be able to distinguish, by delicate electrical tests, the true from the simulated or psychogenic affections of the sciatic nerve. He finds that hyperexcitability to electrical stimulation is not invariably present in the early stages of muscle degeneration, but that decreased excitability and fibrillary contractions of minimal current strengths are equally important evidences of early organic disease of the nerve. This latter type of reaction was never observed in the hysterical sciaticas.

**LABORATORY EXAMINATIONS.**—Unless there is evidence of a metabolic or internal medical disorder, the customary examinations of the blood and urine show slight, if any, variation from the normal. Occasionally, however, a positive Wassermann reaction is obtained in the blood-serum, but, in most instances, the test is thought to be of little etiological significance. Nevertheless, the studies of Boudet, already referred to, seem to indicate that syphilis cannot be entirely excluded as an etiological factor; and some clinicians are of the opinion that an unexplained lumbosacral radiculitis is strong presumptive evidence of its luetic origin. It is in this type of the affection that the serum Wassermann reaction is most likely to be positive.

Further confirmation of this belief is found in the studies of the spinal fluid by Sicard and Roger, Leri, Boudet, A. Thomas and others, who have noted moderate lymphocytosis and increase of globulin as fairly constant findings in the so-called high type of sciatic involvement. The sodium chloride and carbohydrate percentage in the fluid were, however, unchanged; and in only 3 of the 32 cases, studied by Sicard and Roger, was a positive Wassermann reaction obtained. In one instance both the blood and spinal fluid were positive, while in 2 cases a fixation test was obtained in the blood alone. Notwithstanding the frequent occurrence of lymphocytosis and a strongly positive globulin reaction, Sicard and Roger do not agree with the opinion expressed by Boudet and Déjerine; but rather maintain that syphilis is an extraordinary cause of sciatica.

The roentgenogram is, in the so-called idiopathic or primary affection, of little diagnostic aid, except as a means of exclusion, and the picture secured in many of the arthritic sciaticas is often misleading; this seems to be especially true of the slighter degrees of pelvic injury, and in the minor sacro-iliac arthritides. Nevertheless, in every instance, careful x-ray studies should be made.

**Diagnosis.**—The secondary sciaticas offer little diagnostic difficulty. The character of the pain, the nerve tenderness, the condition of the reflexes, and the presence of Valleix's points, or one or more, of the various signs usually serve to establish a correct diagnosis. It is necessary, however, to distinguish the affection from diseases of the hip, arthritis, of the lumbar spine, and injury or diseases of sacro-iliac joint. The limitation of movement, the production of pain upon palpation or manipulation of the joint, the rigidity or atrophy of the extensor muscles, the absence of nerve tenderness, and the x-ray are helpful differentiating features in disease of the hip-joint; and a history of injury, tenderness over the joint, the x-ray, and Patrick's test are of value in distinguishing affections of the sacro-iliac synchondrosis. Tumors of the spinal cord or of the cauda equina and radiculitis may be recognized, by

the radicular character of the pain and objective sensory defect, the absence of nerve tenderness, the presence of sphincter disorders, the increased pain produced by coughing, and the lymphocytosis, xanthochromia, and globulin content of the spinal fluid. Intermittent claudication and flat-foot present some of the features of sciatica; and the psychalgias and hysterical states often require careful diagnostic consideration. It is stated, however, that genuine sciatica cannot be simulated by the neurotic, although he may magnify the symptoms of the organic disease; since the sign of the great toe, the abolition of the gluteal fold, and the dissociated plantar response are not subject to control by the psychogenic malingerer.

**Complications.**—Ordinarily, the disorder runs an uncomplicated course; but herpes, postherpetic neuralgia, edema, and a secondary ascending neuritis with involvement of the nerve roots, the spinal cord, or the opposite nerve trunk have been described. The sphincter disturbances, which have been attributed to sciatic disease, are usually the result of spinal cord involvement.

**Treatment.**—Rational therapy obviously rests upon a correct interpretation of the clinical and pathological condition, and must be directed toward removal of the exciting cause and the restoration of normal function. Thus, a **thorough examination** is the first essential; and in every instance it should consist of neurological, medical, orthopedic, laboratory, and x-ray investigations. By this means the patient may, in the majority of instances, be referred to the particular department, or specialists most competent to direct the therapy; and not infrequently some form of orthopedic treatment will be found most efficacious.

Whatever the nature of the affection, it is well, at first, to insist upon **absolute rest in bed** for a variable period. If the pain is particularly distressing, counterirritation, a **prolonged hot bath**, the **electric pad**, the **galvanic current**, or the **Paquelin cautery** are often useful, and one or more of the various **analgesics** alone or in combination, may be prescribed; but only in exceptional instances should morphin be administered. Active elimination, sufficient sleep, and in the acute stages, a moderately restricted diet are recommended. The author has seen few cases which were not benefitted by the adoption of suitable mechanical or orthopedic measures; and although there may be no evidence of local infection, no history of trauma, and no confirmation of arthritis roentgenogram, it is desirable, during the rest period, to supplement the medical treatment by fixation of the sacro-iliac synchondrosis with firmly applied adhesive straps.

Various more or less fanciful measures have been recommended for the management of the chronic affection. At one time perineural and epidural injections of normal salt solution, air, novocain, urea hydrochlorid, and alcohol had their advocates. The use of alcohol is vehemently condemned. Leszynsky, Strauss, Hecht, Favini, and others record the successful use of Lange's infiltration method, although Rosenheck and Finkelstein have found it of little benefit. Nerve stretching was once practiced with variable success, and more recently, Renton has recommended nerve-freeing as a more efficacious procedure. It occurs to the author, however, that the latter operation must subject the nerve to a certain amount of trauma which may be productive of fresh adhesions during the process of recovery; Renton has, however, observed

some of his post-operative cases through a period of thirteen years and finds no evidence of a recurrence of the symptoms.

Acupuncture, the violet ray, the high-frequency current, and galvanic acupuncture have been adopted with uncertain success. Goulden is of the opinion that sciatica is dependent upon a disseminated edematous infiltration of the nerve trunk in the form of nodular enlargements, which are especially painful and may be detected by their hypersensitiveness to the faradic current as it is directed along the skin over the course of the nerve. After having thus localized the painful areas, a sterile needle attached to the negative pole of the galvanic battery, is then introduced through the skin to the depth of the nerve. Each painful nodule is, then, punctured and electrified for ten or fifteen minutes with a current strength varying from 2 to 6 milliamperes. Relief is said to be secured within a few minutes after the treatment is discontinued, provided all of the painful nodules have been thoroughly electrified.

The treatment of sciatica may then be summarized in the following manner: (1) Removal of the exciting cause; (2) the general therapy of neuritic or neuralgic affections; (3) the use of local applications; (4) suspension, nerve-stretching and nerve-freeing; (5) the injection or infiltration methods; and (6) orthopedic or mechanical measures. To these may be added, electricity, massage, hydrotherapy, mud baths, spas, balneotherapy, and the specific treatment of the syphilitic type.

**Prognosis.**—Recovery is the rule. The affection is, however, often protracted and may persist, in a chronic form, for many months, although the acute symptoms usually subside within two or three weeks. The average duration of the disease is from four to six months. Unless, however, the importance of complete rest is fully appreciated, the course of the affection may be greatly prolonged.

**Pathology.**—Only occasionally is there an opportunity for gross or microscopic examination of the nerve trunk, so that exact knowledge of the character and location of the lesion remains unknown. It is assumed, however, that the nerve is swollen, hyperemic, and edematous, and exhibits the histological changes characteristic of a perineuritis; while in some instances the clinical features suggest that it has undergone a true parenchymatous degeneration. On the other hand, because of the transient and paroxysmal nature of the pain, the short duration of the illness, and the absence of sensory or motor defects, it is believed that the disorder may be of neuralgic nature without obvious changes in the nerve tissue. Hunt, in 1905, found in the literature 11 cases of sciatica in which the nerve had been studied, and in only 3 of these was there a microscopic examination. To these he adds a fourth case in which the nerve was swollen from the deposit of a gelatinous material in the perineurium. Microscopically, there was no evidence of inflammation, but the arteries were sclerotic and the nerve sheath contained minute extravasations of blood. Syphilis was said to have been excluded, and the lesion was attributed to a gouty diathesis.

## MULTIPLE NEURITIS

Multiple neuritis, polyneuritis, or peripheral neuritis is an acute or subacute affection, principally of the distal portions of symmetrically placed nerves, characterized by sensory and motor disturbances, conse-

quent upon a degenerative and moderately inflammatory lesion of toxic or infectious origin. The spinal cord, the heart, and the striated musculature occasionally suffer in the general intoxication.

With the exception of an occasional wide-spread epidemic, such as that described by Reynolds in the English beer-drinkers, and certain endemic forms of the disease, multiple neuritis is, relative to the large number of etiological factors, a comparatively uncommon disease. Ordinarily, the two sexes are about equally affected, but the alcoholic type is said to be more common in women. The disorder is more frequent in the second, third, and fourth decades; and although the peripheral nerves may be involved in poliomyelitis and in diphtheria, children are not, as a rule, particularly susceptible to the usual forms of multiple neuritis. The aged are sometimes affected with a rare senile, or atheromatous polyneuritis.

**Types of Multiple Neuritis.**—Various attempts have been made to classify the disease upon a clinical, an anatomical, an etiological, or a pathological basis. Thus, it was customary to speak of an alcoholic, an arsenical, an ataxic, a motor, a sensory, and a mixed neuritis. Degenerative, inflammatory, and recurring types were also recognized; and, more recently, a neuronitis has been described, in which the entire lower motor neurone is affected. The manner in which the toxin is thought to be conveyed to the nerve tissue has been responsible for the recognition of a hematogenous, a lymphatic, and a specific neural form of the disease; but recent studies have shown that distinctions of this character are not altogether warranted, and it is now generally acknowledged that polyneuritis is a disease of toxic or infectious origin; that no constant specific clinical type can be identified; and that the pathology of the various forms of the disease is quite indistinguishable.

It is, accordingly, more acceptable to classify the disease into two principal etiological divisions: A toxic form of chemical origin, and an infectious type resulting from the bacterial poisoning accompanying the specific diseases. In the first group the toxin may be of exogenous or endogenous origin; and the more common exogenous toxins are derived from such organic and inorganic chemical substances as alcohol, the coal-tar preparations, lead, arsenic, copper, mercury, silver, phosphorus, and carbon monoxid; while the endogenous toxins, usually of metabolic or dietetic origin, are frequently the result of diabetes, gout, anemia, the cachexia of tuberculosis or cancer, the so-called rheumatic diathesis, and the nutritional disturbances occurring in beri-beri.

Of the infectious diseases, diphtheria, influenza, and typhoid fever, are those most often complicated by a peripheral neuritis; and, occasionally, the affection has developed as a sequence of scarlet fever, malaria, puerperal infection, small-pox, and parotitis. A gonorrheal and a syphilitic neuritis have also been described; and, recently, an acute toxic polyneuritis of infectious origin has attracted wide attention, and will be more fully described as a separate type. Direct infection of the nerve trunk is uncommon, and occurs in its most characteristic form in leprosy. The gonococcus and the spirochete are also said to produce a specific lesion of the peripheral nerves. In all probability, the hypertrophic interstitial neuritis of Déjerine and Sottas belongs to this type of the disorder, but some writers prefer to include it among diseases of the spinal cord.

Finally, there remains a small group, in which searching inquiry fails to reveal any of the better known etiological factors, and it is

accordingly designated as an idiopathic or rheumatic type of neuritis probably dependent upon cold, exposure, and dampness.

It is convenient, then, to arrange the more familiar types of polyneuritis according to the following tabulation:

1. Multiple Neuritis of Toxic Origin.
  - (a) The exogenous toxins of a chemical nature: Alcohol, coal-tar preparations, lead, arsenic, silver, mercury, copper, phosphorus, and carbon monoxid.
  - (b) The endogenous toxins of metabolic or dietitic origin: Gout, diabetes, anemia, the cachexia of tuberculosis and cancer, and the nutritional disorder in beri-beri.
2. Multiple Neuritis Resulting from the Toxemias of the Infectious Diseases. Diphtheria, influenza, typhoid fever, scarlet fever, malaria, puerperal fever, septicemia, small-pox, parotitis, and probably, gonorrhea and syphilis.
3. Acute Toxic Febrile Polyneuritis.
4. Multiple Neuritis Due to Direct Involvement of the Nerve Trunks. Leprosy, and probably the hypertrophic interstitial neuritis of Déjerine and Sottas.
5. Multiple Neuritis of Unknown Origin. Exposure, cold or rheumatism.

**Etiology.**—Although many of the more familiar toxic agents have already been mentioned in the description of the various types and classification of the disease, some of them deserve further consideration; and there are, in addition, other factors which were not included in the preceding tabulation.

Arsenical intoxication may be derived from a variety of sources, and Moreau has described an interesting form of poisoning resulting from the inhalation of arsenated hydrogen liberated on board a submarine. Twenty members of the crew suffered from mild toxic symptoms; while, in one instance, the patient developed, three days after exposure, complete motor paralysis of both legs, and the right shoulder and arm. The legs recovered completely, but paralysis of the circumflex and supra-scapular nerves persisted for many months. Neuritis due to zinc poisoning is, according to Marie, not an uncommon type; and, as in some cases of arsenical poisoning, the zinc may be derived from the use of impure sugar in the fermentation of wines and beers. Morphinism is, in Oppenheim's opinion, an occasional etiological factor, from which the symptoms may arise during the use of the drug or following its withdrawal.

Carbon monoxid poisoning has been assigned as a cause of polyneuritis, but there is some uncertainty as to whether the lesion is of toxic or mechanical origin. It is thought that pressure upon the nerve trunks, resulting from abnormal positions of the extremities during the comatose state, may be a contributing factor. Veraguth has described a case of carbon monoxid polyneuritis, in which the poison was derived from the ignition of a number of graphophone records in a closed room. The unconscious patient remained in a cramped position for twenty-four hours when it was discovered that both legs, the right face, and the shoulder muscles were paralyzed. In another instance the polyneuritis was attributed to "solvent naphtha" used in the automobile industry; and in a third case, of the Korsakow type, the disorder was thought to be due to the bacillus botulinus. Physical agents are, according to Sterling, sometimes the cause of multiple nerve symptoms, and he reports a case in which the affection was apparently the result of lightning-stroke.

That typhoid fever is responsible for degenerative changes in the peripheral nerves is questioned by Feiling, who states that he has never seen a well-marked case. Peripheral neuritis is, however, said to occur in paratyphoid fever, in pneumonia, and in hemophilia; and Harris has recorded an unusual instance of the affection occurring in leukemia, in which the polyneuritic symptoms developed sometime before changes were noted in the blood-picture. Microscopic examination revealed a leukemic lymphocytic infiltration of the nerve trunks, although both the leukemia and the neuritis were thought to be of toxic origin.

The belief is general that the peripheral nervous system is not affected by the tetanus toxin, but Richardson has observed multiple involvement of the nerves during the course of the disease. The patient had received a total dose of 150,000 units of antitoxin. During the course of treatment, administration of the antitoxin was occasionally followed by an anaphylactic reaction and, in one instance, by local infection at the seat of injection. Richardson suggests, therefore, that the neuritis may have been due to the tetanus toxin, to the antitoxin, or probably, to the local secondary infection. The author has, however, seen 2 cases of facial diplegia in patients who were receiving tetanus antitoxin. In both instances secondary infection was definitely excluded, and the paralysis occurred several weeks after the treatment was discontinued.

Exposure, from prolonged standing in cold trench-water during the recent War, was thought to be of etiological importance in a case of polyneuritis described by Pophyllat. Both feet were severely frost-bitten, but no mention is made of infection. Eight days after the exposure, progressive neuritic symptoms developed in both legs, and finally implicated the arms in a symmetrical fashion, although the upper extremities were well protected from the weather.

A gastro-intestinal or enterotoxic condition is, in all probability, an occasional cause of multiple neuritis. Feiling has observed a mild type of the affection in one suffering from bacillary dysentery, and Kilgore attributes the disorder, occurring in 5 members of the same family, to the use of emetin in the treatment of anebic dysentery. Oppenheim includes dysentery among the etiologic factors, while Barker and Estes have described an interesting polyneuritic syndrome and tetanoid attacks, associated with chronic dilatation of the stomach and duodenum.

There is reason to believe that some unknown factor other than the original intoxication may be responsible for the development of the neuritis, since it is difficult to imagine that each of the large number of toxic substances should exhibit a special affinity for the peripheral nerves; hence, it is believed, that in some instances, the nerve lesion is due to an hepatic poison consequent upon destructive changes in the liver resulting from the primary intoxication; and it is, of course, well known that certain chemical substances, particularly the heavy metals, may produce necrotic changes in the liver. Sainton has described a case of polyneuritis associated with gray hepatic degeneration, while the syndrome attributed by Klippel and, later, by Donnet to hypertrophic cirrhosis of the liver bears a close resemblance to the well-known Korsakow paralysis. Since many of these patients were addicted to the use of alcohol, it is difficult to attribute the neuritis directly to the changes in the liver; and more convincing evidence is, therefore, needed to establish a hepatogenous type of multiple neuritis.

Syphilis as a cause of neuritis continues to be a much-discussed subject, although evidence is accumulating which suggests that lues may be an occasional etiological factor. A critical review of the subject by Oppenheim, in 1890, did not enable him to arrive at a definite conclusion as to whether the primary infection, or the specific treatment was the cause of the neuritis. Petren has since made a postmortem study of a syphilitic patient who had exhibited polyneuritic symptoms. The syphilis was of six months' duration, and intensive treatment had resulted in evidences of mercurial intoxications, to which the fatality and the neuritis were attributed. Nevertheless, Petren concludes, from this observation and from a review of the literature, that syphilis is an occasional etiologic factor; and that the neuritis occurs most frequently during the first year of the infection, although it may develop during any period from the first month to the twenty-sixth year. In one instance the symptoms developed in a congenital syphilitic, and H. M. Thomas and Greenbaum found 2 additional cases of the syphilitic type among the multiple neuritides occurring in children. Several instances have been recorded by Fordice, Fournier, and Cestan in which a well-marked polyneuritis has been apparently relieved by intensive anti-luetic therapy.

The introduction of arsphenamin in the treatment of syphilis has contributed a new etiologic factor, and added to the difficulty of distinguishing a specific, from a therapeutic type of multiple neuritis. That the affection is sometimes observed during or following arsphenamin therapy is now generally recognized; and Beeson finds that, although the neuritic symptoms may develop after only one dose of the drug, they appear more frequently upon the completion of a series of treatments and, ordinarily, not until two or three weeks after the therapy has been discontinued. Occasionally, the neuritis may precede, accompany, or follow an associated arsenical dermatitis. Nevertheless, when one considers the extensive use of arsphenamin, polyneuritis is a comparatively rare complication incident to its administration.

**Symptoms of Multiple Neuritis in General.**—The clinical history, as in many nervous affections, is of special importance. Careful inquiry should be made in regard to the patient's occupation and likelihood of exposure to the various chemical agents which are known to be responsible for degenerative changes in the peripheral nerves. A history of a preceding infectious disease is not infrequently obtained, and the nutrition, diet, metabolism, previous medication, and alcoholic indulgence are to be closely investigated. Ordinarily, it is not difficult to establish a very definite relation of the symptoms to one of the many etiological factors enumerated in the classification and etiology of the disease.

Of the earlier symptoms, weakness, particularly of the lower extremities, pain, numbness, tingling, and undue fatigue are the most significant; and whatever the origin of the disease, these sensory and motor disturbances are almost invariably bilateral, symmetrical, and confined to the distal portion of the extremities. Cutaneous hyperaesthesia is often a prominent symptom; and general malaise, gastrointestinal disorders, cardiac arrhythmia, and moderate rise of temperature sometimes initiate the disease. Muscle tenderness is a characteristic feature, and, in the beginning, may be the cause of apparent motor weakness. The gait is of a "steppage" type, and possesses additional distinctive features to which Dr. Spiller has directed the author's atten-



tion. Thus, the feet are lifted well above the surface; but, unlike the usual "steppage gait," descend with the heel first, followed by a tapping sound as the toes of each foot strike the floor. Since the affection is bilateral, the patient walks in "common" or "four-four time" with perfect rhythm, which may be audible for some distance on an uncovered floor. The arms are also affected, and occupy the position characteristic of the familiar wrist-drop. As the disease progresses, atrophy, the reaction of degeneration, loss of the tendon reflexes, contracture, objective sensory defects, and trophic changes are added to the symptomatology; and ataxia, tremor, and psychic disturbances are special features in certain types of the disease.

**SENSORY SYMPTOMS.**—As a rule, the sensory changes make their appearance early in the course of the affection; and, according to Grinker, this is particularly true of the alcoholic and arsenical types. These symptoms may, however, be entirely subjective and transitory, so that the motor paralysis constitutes the entire clinical picture. Feiling finds the motor type especially common as a post-influenzal affection; and it is well-known that the sensory fibres rarely suffer in the neuritis following diphtheria and lead poisoning. On the other hand, Pryce has observed a purely sensory multiple neuritis resulting from a cancerous cachexia.

At the outset, variable degrees of pain, tingling, numbness, and paresthesia are common. As a rule, the pain is constant, occasionally of a shooting character, and marked by nocturnal exacerbations. Nerve tenderness is often present, and is an important feature in distinguishing the affection from *tabes dorsalis*, in which the pain is frequently mistaken for that of neuritis. The deeper tissues are also acutely sensitive, and muscle tenderness is generally regarded as a diagnostic symptom of peripheral neuritis. It is especially marked in the alcoholic type, and to so great a degree in the arsenical form, that Marie regards the symptom as a means of differentiating the two types of intoxication.

Objectively, all forms of cutaneous and deep sensibility may be involved, but the ability to recognize light touch appears to suffer more constantly and more severely; while the sense of position and muscle sense are particularly affected in the ataxic form of the disease. Delayed transmission of sensory impression has long been regarded as one of the early evidences of locomotor ataxia, but Grinker has made the important observation that this form of sensory defect is also an occasional symptom in multiple neuritis. When the anesthetic area is fully developed it is nearly always symmetrical, and occupies a region upon the distal portions of the upper and lower extremities comparable to that covered by the gloves and stockings; thus, it is, accordingly, designated as the stocking and glove type of sensory loss.

The inaccuracies attending examination of the vibration sense, and Symns's method of obviating them by use of a specially devised tuning-fork, have been referred to in a previous section. Symns has studied the vibration sense in a variety of nervous diseases and finds that it is the only form of sensation which is constantly defective in diabetic neuritis; that in the lead, alcoholic, and diabetic forms its diminution always precedes loss of the knee-jerks; and that, in the sacral region, diminution or loss of the vibration sense is uniformly observed in *tabes*, although this area is never affected in multiple neuritis. Williamson describes loss of the vibration sense as an early symptom of alcoholic neuritis, but finds it preserved in isolated nerve lesions, although all

other forms of cutaneous sensibility may be abolished. Wood, of Wilmington, North Carolina, has recently made a series of tests with the Symms's tuning-fork and concludes that, examination of the vibratory sense is a helpful diagnostic procedure by means of which it is possible to determine in certain nervous affections a more or less specific period of duration for the perception of the vibrations. Confirmation of his studies will, no doubt, furnish a valuable means of differentiating spinal cord and peripheral nerve affections.

**MOTOR SYMPTOMS.**—The motor neurone is often severely affected, and fatigue, motor weakness, and muscle tenderness may even precede the onset of sensory symptoms. The paralysis conforms to the anatomical distribution characteristic of the disease. As a rule, the legs are first affected, and the tibial and peroneal group of muscles, the calf muscle, and finally, the muscles of the thigh are successively involved. In some instances, atrophy may be pronounced from the beginning but, according to Marie, it is never so intense as that occurring in the progressive central muscular type; and only rarely is it confined to the small muscles of the hands. With the progress of the disease, the extensor muscles of the wrists and fingers become involved; so that, in addition to the bilateral foot-drop and steppage gait, there is symmetrical drooping of the wrists; and subsequently, the flexor muscles in the forearm and the intrinsic muscles of the hands take part in the wide-spread atrophic changes.

Usually, the muscles of the shoulder girdle and those of the upper arm escape, but Feiling has found the paralysis confined largely to this group of muscles in a case of polyneuritis following typhus fever; and Sainton has described an instance of a combined lead and alcoholic neuritis, in which the paralysis was at first limited to both upper extremities. There were no sensory changes; the brachioradialis and the interossei were not involved; and an unmistakable lead line was detected in the gums. The subsequent development of psychic disturbances and bilateral foot-drop was attributed to the alcoholic intoxication. Oppenheim has observed 2 cases of multiple neuritis of unknown origin in which the paralysis was also confined to both upper limbs, and Grinker refers to the occurrence of an upper-arm type of polyneuritis in lead poisoning. The muscles of the trunk are said to be rarely affected; but the diaphragm and abdominal muscles are sometimes involved; and Feiling finds them not infrequently affected in the post-influenzal type of multiple neuritis.

During the early stages of the disease, before the appearance of paralytic and atrophic symptoms, irritative motor phenomena are occasionally observed. Thus, tremor, and spasmodic, painful contractions of the muscles, particularly in the arsenical and alcoholic types, are not uncommon features, although true fibrillation is said not to occur. In well-marked cases, atrophy, the reaction of degeneration, and contracture make their appearance; and ataxia is sometimes a prominent symptom. The author has described an ataxic form of neuritis, in which loss of the vibratory sense added to the difficulty in distinguishing the affection from genuine tabes dorsalis.

**THE CRANIAL MOTOR NERVES.**—With the exception of the diphtheritic paralyses, the cranial nerves are only occasionally implicated in the polyneuritic syndrome. It appears, however, that the seventh, or facial nerve is most frequently involved, and, as a rule, the lesion is bilateral. Patrick, in 1916, reported two instances of the affection, and collected

from the literature 45 additional cases. It is his opinion that, when the facial nerve is involved, the neuritis of the extremities is less intense. Spiller, Dana, and Leopold have also noted facial diplegia as part of a symmetrical neuritis, and Oppenheim has seen paralysis of the soft palate and vocal cords in polyneuritis of infectious origin. Ocular palsy, strabismus, nystagmus, and hypoglossal paralysis are occasional symptoms, and Sainton has, in one instance, observed paralysis of the motor portion of both trigeminal nerves.

**SPHINCTER DISORDERS.**—It has been generally taught that paralysis of the sphincters forms no part of the clinical picture of multiple neuritis. Nevertheless, unquestioned instances of sphincter involvement have been observed in what must otherwise be regarded clinically, at least, as typical neuritis; and yet, loss of sphincter control, at once, necessitates a review of the diagnostic data. It was not then fully understood that multiple neuritis is only one of the manifestations of a general intoxication in which the central nervous system is sometimes affected. There is, then, no reason why sphincter paralysis may not be occasionally added to the more familiar symptoms of the disease, and it appears to be Patrick's opinion that it need not be of central origin; since there is no proof that the peripheral nerves to the bladder and rectum escape the degenerative changes characteristic of multiple neuritis. Marie maintains, however, that sphincter paralysis is never of peripheral origin.

**THE REFLEXES.**—The pupillary reaction is said to be occasionally affected. Grinker finds transient retardation of the light reflex not uncommon, and paralysis of accommodation is a characteristic feature of the postdiphtheritic type of neuritis. Even the typical Argyll-Robertson pupil is said to have been noted in a case of alcoholic polyneuritis. The blood Wassermann test was negative and venereal infection denied; but clinical histories are often unreliable, and alcohol is known to inhibit the Wassermann reaction, so that, in this instance, it is difficult to exclude syphilis as a contributing factor. Feiling and Viner have noted iridocyclitis and parotitis in association with multiple neuritis, although the nature of the affection was undetermined.

In the acute stages of the disease, the tendon reflexes may be hyperactive, especially when there is an associated affection of the spinal cord, but, as the lesion becomes destructive, they are diminished and finally lost. Usually, the knee-jerks are the first to be affected and, in severe cases, all of the deep reflexes are subsequently involved. Restoration of the tendon response to normal activity is invariably delayed for many months after the disappearance of all other symptoms. The cutaneous reflexes are said to be unaltered, but it is reasonable to suppose that, if the area in which the reflex is ordinarily elicited be entirely anesthetic, no response will be obtained.

**TROPHIC AND VASOMOTOR SYMPTOMS.**—Trophic disturbances are not, ordinarily, prominent features of the disease; they are, however, more likely to develop when the neuritis is of long standing. Bed-sores are uncommon, although the milder cutaneous and vascular changes are not, in Marie's opinion, of infrequent occurrence. Thus, the skin of the affected part may be wrinkled, thin and shiny, or rough and thickened; and, sometimes, local sweating is profuse. In the arsenical and diabetic neuritides, the skin lesions are often pronounced and characterized by trophic changes in the nails, exfoliative dermatitis, and perforating ulcer.

Occasionally, the extremities are swollen, especially about the hands and feet, and Gowers refers to the occurrence of a brawny edema. The surface temperature may be reduced, or there may be subjective sensations of heat and cold; and, when the neuritis is due to one of the metallic poisons, the skin is sometimes cyanotic, congested, or pigmented. In rare instances, the symptoms of Raynaud's disease have developed, or the paralyzed limb has become gangrenous. The swollen, edematous condition of the joints is attributed to trophic changes but, in all probability, these symptoms are dependent upon the general intoxication.

**MENTAL DISTURBANCES.**—The psychoses are more common in the alcoholic polyneuritides; and, in the severer forms, Korsakow has included, among the characteristic features, loss of memory for recent events, fabrication, disorientation, hallucinations, delusions and, occasionally, complete dementia. This degree of mental aberration is, however, not always fully developed, nor is the so-called Korsakow syndrome confined to the alcoholic type; it is occasionally encountered in the lead, arsenical, and septicemic forms of neuritis; and Foggie has observed it, associated with hyperemesis, in a case of multiple neuritis consequent upon the toxemia of pregnancy. Variable degrees of psychic disturbance have also been noted in the posttyphoid, influenza, and diabetic neuritides; and Carlill records the appearance of the complete Korsakow syndrome in malarial polyneuritis. But the Korsakow psychosis may develop independently of the neuritic process, and the author has observed this dissociated syndrome in a patient subject to chronic alcoholic overindulgence.

**Diagnosis.**—Although multiple neuritis presents features common to a variety of nervous affection, recognition of the disease is, under ordinary conditions, not difficult; but Feiling has correctly stated that the diagnosis should not be regarded as fully established until the etiology has been determined.

Clinically, the disease is characterized by the peripheral, symmetrical disposition of the paralysis which appears first, in the lower extremities, and then in the forearms without, as a rule, involving the trunk. The character of the pain, the nerve and muscle tenderness, and the gait are more or less distinctive; and the paresthesia, the skin changes, and the configuration of the anesthetic area contribute to the details of the clinical picture. Preservation of sphincter control and the absence of fibrillary contractions are said to be important differentiating features.

It may be difficult, at times, to distinguish the ataxic form of the disease from tabes dorsalis; although, in the latter condition, the lightning pains, the pupillary changes, the optic atrophy, the various crises, the irregular distribution of the sensory defects, the sphincter disturbances, the girdle sensation, and the absence of nerve or muscle tenderness should enable one to arrive at a correct diagnosis. Muscular atrophy, an important symptom in multiple neuritis, has also been observed as a rare complication of tabes; and, as a further means of differentiation, a careful search should be made for the irregular areas of tabetic retardation of pain sense on the thoracic wall; and although this type of sensory defect may occur in multiple neuritis, the hypalgæsic areas have a different configuration, and are not situated upon the thoracic or abdominal regions. Notwithstanding the probable occurrence of a true syphilitic neuritis, and the occasional discovery of moderate pleocytosis in other forms of polyneuritis, examination of the blood and spinal fluid will more often serve to establish the tabetic nature of the affection.

Although progressive central muscular atrophy exhibits, in common with multiple neuritis, a certain degree of muscular wasting, it may be readily distinguished by the more gradual onset, the absence of nerve or muscle tenderness, and the preservation or increase of the tendon reflexes. Cutaneous sensibility is unaffected; pain is not a feature of the disease; and, later, evidences of upper motor neurone involvement make their appearance. Furthermore, the atrophy, which appears first in the small muscles of the hand, is a symmetrical and often more advanced than that ordinarily observed in multiple neuritis. A lower spinal type of progressive central muscular atrophy has, however, been described. Fibrillary tremor is also a common symptom.

Poliomyelitis, in its acute stage, may enter into the diagnostic problem, since motor paralysis and pain are sometimes dominant features; but poliomyelitis is, more commonly, a disease of childhood; the onset is more acute; constitutional disturbances are often present; and the paralysis is sudden, wide-spread, asymmetrical, and shows an early tendency to partial recovery. The motor symptoms are rarely bilateral, nor are they confined to the distal portion of the extremities. The posterior roots are occasionally affected, but this extension of the process is not productive of the muscle tenderness or sensory defect which characterize the peripheral nerve lesion. Pleocytosis is also an important differentiating feature.

In view of the modern teaching concerning the pathology of multiple neuritis, it seems that the distinction between peripheral neuritis and radiculitis is largely of academic interest. Nevertheless, Williams has prepared a helpful diagnostic table in which the symptoms of the two affections are contrasted. He finds that, the latter condition is more frequently the result of syphilis, vertebral disease, or neoplasm, and that it may be distinguished by the radicular character of the pain, and the segmental distribution of the sensory and motor paralysis. Nerve and muscle tenderness are inconspicuous, and trophic changes are uncommon; but sphincter disorders are not infrequent, and the spinal fluid often shows evidence of the meningeal or radicular lesion.

Acute ascending paralysis, or Landry's palsy, formerly regarded as a distinct affection of the peripheral nerves, was thought to possess features which distinguished it from the usual forms of multiple neuritis; but from recent investigations it appears that Landry's paralysis, acute febrile polyneuritis, and infective neuronitis belong to a specific type of disseminated infection of the entire nervous system in which clinical differentiation is, oftentimes, quite impossible, and without scientific foundation.

Finally, it may be well to caution the reader that arthritic muscular atrophy, and hysteria may simulate a genuine neuritic disorder. In the latter condition, the history, and the discovery of other ear-marks of the hysterical state usually serve to establish the diagnosis; and, in both the psychogenic and arthritic affections, an electrical examination reveals a normal, or only quantitatively altered muscle response.

**Complications.**—Since multiple neuritis can no longer be regarded as a specific nerve affection, it is obvious that the extent and character of the complications and associated extraneural symptoms will depend, to some extent, upon the nature and intensity of the general intoxication. The heart is not infrequently involved, either through disease of the vagus nerve or by direct injury to the cardiac muscle; so that tachycardia, arrhythmia, and myocardial or endocardial changes are

sometimes added to the neuritic symptoms. Occasionally, paralysis of the diaphragm increases the danger of pulmonary complications and the development of a terminal pneumonia; and involvement of the spinal cord or vital nerve centers contributes to the gravity of the situation. The gastro-intestinal, hepatic, and renal complication in the alcoholic type, and the acidosis in the diabetic form of the disease render the outlook more serious.

**Treatment.**—If the nature of the toxin be determined and its elimination accomplished, the course of multiple neuritis is largely self-limited and, under ordinary circumstances, proceeds slowly to a favorable termination; thus, the first object of successful therapy is directed toward the **management of the primary intoxication**. In many instances, then, the treatment of multiple neuritis is, in reality, the treatment of alcoholism, of diabetes, of influenza, of the anemic and cachectic states, and of the various chemical intoxications; and this aspect of the therapy should be directed by a competent internist. There are, however, more specific features of the condition, dependent upon the local changes within the nervous system, which require special therapeutic measures.

Whatever the nature of the toxin or the extent of the neuritis, **complete rest** in bed is essential; and, at first, voluntary movement of the affected parts should be interdicted. A soft mattress or a water-cushion will add to the patient's comfort; and when hyperesthesia is particularly distressing, the bed-clothes may be supported by a cradle. The elbows and knees are to be maintained in extension, if necessary by moderate traction, and the feet should be supported in slight flexion by a padded sand-bag placed against the foot of the bed, while flexion at the wrists is to be obviated by the use of well-cushioned splints.

After these general measures have been attended to, **active elimination, sufficient sleep, and suitable diet** should be secured. Liberal internal hydrotherapy is a valuable means of elimination and, unless there are special indications, any well-balanced diet will be suitable; Williams, however, prefers one of low protein content, but rich in salines. Insomnia, when present, is generally due to pain or other sensory discomforts, so that it may be necessary to resort to the use of sedatives, analgesics, or hypnotics, unless the milder forms of external hydrotherapy prove efficacious.

In the acute stages, massage, active or passive movements, and tension upon the paralyzed muscles are to be avoided. Occasionally, the **mild galvanic current** temporarily diminishes the intensity of the pain, or else the affected part may be wrapped in a warm moist dressing, or in cotton-wool, or bathed by cool, gentle sponging. **Veronal**, or a combination of the drug with **aspirin**, is said to be of use in relieving the muscle spasm. Starr finds large doses of the salicylates of much value, and phenacetin, pyramidon, and allonal have their special advocates. Morphine should be prescribed only in cases of necessity, and alcoholic beverages are to be avoided. During convalescence, it is customary to order a **general tonic course**, in which strychnin, iron, and arsenic are the favorite preparations. Unless the etiology of the disease is definitely established, it may be well to withhold the use of arsenic; since the author once saw a patient, with a severe polyn neuritis, who was receiving daily administrations of the drug until it was later determined that the neuritis was of arsenical origin.

It has been generally believed that, in lead poisoning, the elimination of the metal is facilitated by the administration of potassium iodid,

but Dixon Mann has shown that there is no foundation for this belief. Felling recommends the use of the double electric bath. Neuritis occurring in pregnancy is, in Foggie's opinion, no indication for the interruption of gestation, unless there is evidence of profound toxemia or serious cardiac embarrassment.

Throughout the course of the disease every precaution should be taken against the development of secondary contracture and, as the acute symptoms subside, the skilful use of electricity, massage, and passive movements will do much to prevent its occurrence; but in case these measures are not effective, some form of orthopedic or surgical procedure may be adopted.

**Prognosis.**—Under favorable conditions, if the disease is recognized early and the toxic agent eliminated, the prognosis for recovery is good. The development of contractures is an unpleasant complication, although Marie finds this circumstance not entirely beyond alleviation. Disease of the heart muscle and respiratory paralysis make the prognosis more ominous, and, sometimes, result in a fatal termination. Thus, the disease should not be regarded lightly, or a too hopeful prediction announced when the symptoms are of unusual severity; and the prognosis is to be especially reserved in acute febrile polyneuritis, in the edematous form of beri-beri, and in the postdiphtheritic type of the disease. According to Pitres and Marchand, neuritis of diabetic origin usually terminates favorably, although the prognosis depends largely upon the readiness with which normal metabolic conditions may be established.

In its usual form, polyneuritis runs a prolonged course, extending over a period of many months, and recovery, at best, is slow. Spiller has studied the order in which the muscles of the lower extremities regain their function, and finds that the long extensor of the great toe and the tibialis anticus are the first to recover; but, with the exception of the arsenical type, cutaneous sensibility returns before voluntary movement and loss of the tendon reflex is, as a rule, the last symptoms to disappear.

**Pathology.**—The epidemic of influenza during 1918, the subsequent occurrence of acute encephalitis, the recognition of an acute febrile polyneuritis, the discovery of a true neuronitis, and the studies of Orr and Rows upon lymphogenous pathways of infection have contributed largely to a modification of the older views concerning the pathology of multiple neuritis. It is now generally admitted that the disease can no longer be regarded as a true inflammatory affection confined to the peripheral nerves, but that the nerve lesion is only part of a general systemic intoxication in which the brain, the spinal cord, the heart, and the skeletal muscles also frequently suffer.

Sainton has described an interstitial inflammatory reaction in the nerve trunk, although the characteristic lesion is represented by a true parenchymatous degeneration not unlike the Wallerian type. The degeneration is, however, more disseminated than that following nerve section, and is especially marked at the periphery. Occasionally, the nerve exhibits a moderate degree of congestion and variable round cell infiltration; and upon gross examination it may be edematous and slightly congested, but as a rule, the lesion is of a microscopic nature. Although Marie and others have demonstrated associated changes in the central nervous system, Sir David Ferrier is of the opinion that, notwithstanding the occasional involvement of the brain and spinal cord,

the extensor motor axones of the peripheral nerves unquestionably suffer most severely.

### SPECIAL FORMS OF MULTIPLE NEURITIS

Because of the older belief that the several types of multiple neuritis possessed a distinctive pathology and symptomatology, it was customary to describe, in detail, the features thought to be characteristic of the various intoxications. It is now generally accepted, however, that the pathology of the affection shows little variation in the several types, and that the differential symptomatology depends more upon the earmarks of the specific intoxications, than upon any peculiarity in the order or sequence of nerve symptoms. Thus, while the majority of cases conform to the general description of the disease, some of the better-known types, occasionally, present features suggestive of the particular form of intoxication.

**Alcoholic Neuritis.**—The affection is said to have been first described, in 1822, by Dr. J. Jackson, of Boston. The symptoms are more frequently induced by the prolonged use of distilled spirits, than by the occasional excesses of the periodic drinker. In rare instances, the fumes of alcohol are said to have been responsible for the neuritis. The fermented liquors, with the exception of beer, are uncommon sources of intoxication; and the well-known studies of Reynolds in 1900, have shown that the epidemic among the English beer-drinkers was, really, not of alcoholic origin, but due to arsenical contamination of the sugar employed in the process of fermentation. These studies have led to much discussion as to whether alcohol is an actual cause of neuritis or merely a predisposing factor; and although its exact etiologic position has not been determined there are numerous instances in which no other etiologic factor was disclosed. Nevertheless, alcoholic polyneuritis is, relative to the wide-spread use of distilled liquors, a comparatively uncommon disease. Feiling finds it occurring with diminishing frequency. The condition is said to be more common in women, whose custom it was, until within recent years, to confine their steady tipping to the privacy of the boudoir, where cologne and other sweet-scented extracts were occasionally used externally and internally for olfactory and cerebral excitation.

The onset of the neuritis may be gradual or acute, and is most likely to develop between the third and fifth decades, although Starr has seen the affection in a child, three years of age which was attributed to the drinking of beer. Usually, after a period of vague sensory disorders or undue fatigue, there may be sudden weakness of both legs which progresses to the fully developed paralysis within a fortnight. The motor disturbance has, however, no distinguishing characteristics. Sensation is often severely affected, and pain and muscle tenderness are pronounced, although not so intense as in the arsenical type. Morning vomiting, gastric irritability, and anorexia, are common gastro-intestinal symptoms; and tachycardia, myocarditis, dyspnea, pulmonary congestion, moderate albuminuria with edema of the extremities, and cirrhosis of the liver, may be added to the neuritic features. As a rule, the extensor muscles are principally affected, and tremor is often pronounced. Visual disorders, nystagmus, extraocular palsy, facial diplegia, and paralysis of the diaphragm and muscles of the trunk have been



observed. Variable degrees of mental derangement are not uncommon, although a psychosis is not distinctive of the alcoholic type, since it may develop in almost any form of polyneuritis; and even the typical Korsakow syndrome has been observed in a variety of intoxications.

**Arsenical Neuritis.**—Arsenic, in Marie's opinion, occupies a position second to alcohol as a cause of multiple neuritis, and in the author's experience, the two affections have occurred with about equal frequency. The drug may enter the system through the skin, by way of the respiratory tract, or through the alimentary canal. Thus arsenical poisoning has resulted from accidental exposure to the fumes or minute air-borne particles of the metal, from the ingestion of the poison with suicidal intent, and from the therapeutic use of the drug in the treatment of chorea, the anemias, and certain skin diseases. Modern intravenous and subcutaneous administrations of a variety of arsenical preparations have furnished additional sources of intoxication. Arsenic is, also, widely used in a number of industries; hence, there are certain trades and occupations in which the individual may be exposed to intoxication. Consequently, arsenical poisoning has occurred in the manufacture of sulphuric acid, in the mixing of certain paints and dyes, and, especially, in the mining and smelting of tin ore; moreover, glass and enamel workers, tanners, furriers, and those engaged in plating are sometimes affected. Wallpapers, carpets, and draperies, especially those of a green color, have been known to contain appreciable amounts of arsenic; and Starr describes a case of polyneuritis in a woman who was confined for a prolonged period, to a room furnished in green cretonne. The draperies were subsequently shown to contain large quantities of arsenic.

The therapeutic use of arsenic has furnished several striking examples of the dangers which may attend its administration, even, in minute doses. H. M. Thomas and Greenbaum have made a study of arsenical neuritis in children who were receiving Fowler's solution for the treatment of chorea. Fortunately, they found the affection not particularly common. Only nineteen instances were recorded in the literature; and in one of them, previously recorded by Osler, the intoxication and paralysis appeared early and terminated fatally after relatively small doses of the solution: Seven drops were administered three times daily for ten days, then discontinued a week, when the same dose was resumed for a period of fourteen days. Although the neuritis is more often the result of chronic arsenical poisoning, Grinker has noted its occurrence after the ingestion of a single small dose of the drug, or it may develop during the course of arsphenamin therapy; and the author has described a severe polyneuritis following acute arsenical poisoning from the ingestion of home-made biscuits, which were contaminated by a baking powder containing large quantities of arsenious acid.

Arsenical neuritis resembles, very closely, the alcoholic type, from which it may be distinguished, only, by the features peculiar to arsenical poisoning in general. Of these, the gastro-intestinal disturbances, the puffiness of the lids, the nasal catarrh, and the changes in the skin, hair and nails are the more important. Fever is not an uncommon symptom, and vasomotor irregularities have been noted. The skin lesions are variable; pigmentation, erythromelalgia, erythema, hyperkeratosis, alopecia, exfoliation, and herpes are the more common forms. Changes in the nails are said to be characteristic. Very often, they are brittle, or ribbed, and Mees describes the presence of a broad white band, due to the deposition of arsenic, which he regards as distinctive. The deposit

is usually observed on all of the fingers, and becomes less marked toward the free edge of the nail. It is said to persist long after the disappearance of all traces of arsenic in the urine. Thus, when the diagnosis is in doubt, chemical examination of the hair, nails, and urine may reveal the nature of the intoxication.

Cutaneous hyperesthesia and muscle tenderness are especially prominent symptoms, and the motor paralysis is often rapid and wide-spread. In some instances, ataxia may dominate the entire clinical picture. It has been stated that the sphincters are never involved, but Grinker has described an instance in which the neuritis was accompanied by a rise of temperature, gastro-intestinal symptoms, and difficulty in emptying the bladder. The course of the disease is usually prolonged.

**Neuritis Due to Lead Poisoning.**—In its natural state, lead occurs chiefly as the sulphid, and often in combination with more valuable metals. Formerly, the acetate was widely used for commercial purposes and in the mixing of paints, but it has since been replaced by some of the salts of zinc. Hence, those engaged in the smelting of ores, plumbers, type-setters, and painters, were not infrequently exposed to lead intoxication. Vaughn refers to a case of poisoning resulting from the use of a cooking utensil which had been repaired with lead solder. The drinking of water which has become contaminated from long-standing in lead pipes, and the ingestion of articles of food previously wrapped in lead foil may be sources of poisoning. The use of cosmetics and certain coloring matters have also been the cause of lead poisoning in a few instances; but probably the most common source of intoxication was formerly due to uncleanness in the handling of food by those engaged in the commercial use of the metal.

The symptoms and diagnostic signs of lead poisoning are familiar to most clinicians. The abdominal pain and obstinate constipation resulting from contractions of the large intestines, the deposition of lead sulphid within the gum margins, the associated anemia, the rise of blood-pressure, the arteriosclerosis, and the basophilic stippling of the red blood corpuscles are characteristic. Headache, and tremor of the tongue, lips, and hands occur frequently; while optic neuritis, delirium, dementia, convulsions, and choreiform movements are common features of lead encephalopathy.

Although there may be wide-spread involvement of the peripheral nerves, the neuritis is more often confined to the upper extremities, in which the extensors of the fingers are first affected; the long extensors of the wrist are next involved, with resulting gradual or sudden appearance of wrist-drop; but the brachioradialis usually escapes, and pain or other sensory disturbances are rarely present. Occasionally, the muscles of the shoulder are affected, and a rare Aran-Duchenne type of palsy, confined to the small muscles of the hand, has been described. The diaphragm, the larynx, and the ocular muscles are sometimes involved; while in the lower extremities, paralysis of the peroneal, tibial and quadriceps muscles is recorded as part of a more extensive lesion.

**Diabetic Neuritis.**—Neuralgia and isolated neuritic symptoms are not infrequent in diabetes, nevertheless the typical symmetrical sensory and motor involvement of all four extremities is of rare occurrence, and contractures are said not to occur. Usually, the neuritis is confined to one or more nerves of the lower extremities, and often in an asymmetrical fashion, or, occasionally, an entire plexus may be involved. Pitres and Marchand have, however, described complete quadriplegia of diabetic

origin. Ataxia, pain, perforating ulcer, and loss of the knee-jerks, in the pseudotabetic type, bear a close resemblance to true locomotor ataxia; and a further analogy to neurosyphilis is seen in the occasional sudden paralysis of the third or sixth cranial nerves. Desquamation of the skin, loss of teeth, herpes zoster, and gangrene independent of arterial thickening, have been attributed to trophic disorders, although not necessarily of neuritic origin. Meralgia paresthetica is an occasional associated symptom. The course of the neuritis is generally of shorter duration than in the alcoholic and arsenical types, but the duration and prognosis depend upon the successful management of the primary condition.

**Diphtheritic Paralysis.**—The frequent paralysis of the soft palate during convalescence from faucial diphtheria has, for many years, been of particular interest to the clinician and pathologist. The affection was formerly attributed to the selective action of the circulating toxin, to a local toxic bath in which the pharyngeal nerves were immersed, or to a true ascending neuritis; but the recent studies of Orr and Rows, demonstrating a perineural lymphogenous pathway of infection to the central nervous tissue, have offered a possible explanation for some of the peculiarities of the diphtheritic paralyses. Walshe has made use of this information in a clinical study of faucial and extrafaucial diphtheritic infections, from which he concludes that the toxin exhibits a local, a general, and perhaps a specific action.

Thus, faucial diphtheria may be the cause of a local pharyngeal paralysis, loss of the accommodation reflex, or a general polyneuritic syndrome, but the extrafaucial infection may also produce three types of paralytic symptoms; hence, in both instances, it is evident that the diphtheritic toxin exhibits a varied *modus operandi*. Walshe has noted that the initial paralysis usually makes its appearance at the focus of infection, but that palatal involvement occurs only in the faucial lesion. He concludes, accordingly, that the essential cause of the paralysis is probably central, and dependent upon a lymphogenous toxi-infection; that the accommodation palsy is due to the specific action of the toxin; and that the ocular symptoms and polyneuritic features are dependent upon a general hematogenous intoxication. It is interesting, in this connection, to recall that, thirteen years ago, M. Allen Starr observed local paralysis of the abdominal muscles as the result of diphtheritic infection of the umbilicus.

The paralytic symptoms, it seems, have no particular relation to the severity of the infection, since they have been known to occur after an almost imperceptible local reaction. Usually, the neuritis does not make its appearance until convalescence is well established, or it may be delayed for a much longer period; and adults are more often affected than children. In the ordinary faucial type of the disease, the paralysis is indicated by the nasal character of the voice, regurgitation, difficulty in swallowing, and loss of the accommodation reflex. The polyneuritic features are not especially characteristic. Both the motor and sensory fibres are affected, although the latter are often involved to only a slight degree. An ataxic type of diphtheritic paralysis has been described; and, rarely, the extra-ocular muscles, or those of the face, neck, and trunk are implicated. Unless, however, the respiratory and palatal muscles are severely affected, a favorable termination of the paralysis may be expected.

**Recurrent Polyneuritis.**—It is, of course, well known that an attack of multiple neuritis does not confer immunity, and there is, accordingly, no assurance that one may not be subject to a recurrence of the affection. Nevertheless, repeated attacks of polyneuritis are comparatively uncommon; and little attention was given to the subject until 1891, when Dr. Mary Sherwood described a recurrent type of the disease. Since then, the disorder has been observed by Ross and Bury, Targowla, Sörgo, Osler, and Bernhardt; and the monograph of H. M. Thomas contains a full description and bibliography of the affection. His patient was first seen in the fifth attack, which was said to differ from the preceding ones, by involvement of the arms in addition to the lower extremities. The five attacks occurred within a period of six years, and usually during the month of June. Each illness was of slow progress, of about six months' duration, and terminated in complete recovery with a free interval of another half year. The cause of the neuritis was not determined; but the patient had been subject to chronic indigestion, and it was suggested that the affection might depend upon a gastro-intestinal or metabolic disorder. Sörgo's case is of particular interest, since he had the opportunity to make a pathological examination which revealed a wide-spread arteriosclerosis of the spinal cord, peripheral nerves, and skeletal muscles. There was some evidence that the condition may have been the result of lead poisoning.

In the cases reviewed by Thomas, the interval between the attacks varied from a few weeks to eleven years. It seems, however, that a return of the affection after the longer intervals does not warrant its designation as a recurrent or relapsing disease; since there is no reason why one, after this extended period, may not be exposed to reinfection or reintoxication from a variety of sources of the same or different nature from that responsible for the initial disorder. Mary Sherwood has, however, excluded recurrence of this character, and has also eliminated all cases in which the nature of the intoxication was established. Thus, the typical disease is said to be of idiopathic or unknown origin, although lead, alcohol, and auto-infection are regarded as of special etiological importance. A recurrent lead palsy is not particularly uncommon and, occasionally, a relapsing alcoholic neuritis has occurred without evidence of reintoxication. Clinically, the affection is characterized solely by its tendency to repeated relapses but, in other respects, does not differ materially from the usual forms of multiple neuritis. The recurrent feature of the disorder has been attributed to the individual susceptibility of the patient and the diminished vitality of the peripheral nerves consequent upon the original intoxication. With this inherent defect in the nerve tissues, it is maintained that the immediate cause of the relapse may be due to the periodic liberation of a specific toxin, or to a secondary poison acting upon the previously injured nerve fibres.

**Progressive Interstitial, Hypertrophic Neuritis.**—Dejerine and Sottas have studied a rare affection, occurring in childhood, characterized by symmetrical, progressive atrophy, beginning in the distal muscles of the lower extremities, and later affecting both hands. The deep reflexes are abolished and the muscles exhibit the reaction of degeneration, but fibrillary tremor and contractures are said not to occur. Cutaneous sensory disorders and ataxia are often present. The nature of the disorder is not fully understood; and it has, at times, been regarded as a form of progressive central muscular atrophy, a Charcot-Marie type of

dystrophy, and a peroneal form of muscular atrophy. Dejerine claims, however, that it may be distinguished from these several types of muscular wasting, and is dependent upon a definite lesion of the peripheral nerves. Nevertheless, it continues to be regarded by many neurologists as a spinal cord affection.

**Acute Febrile Polyneuritis and Neuronitis.**—Within the past five years the bacteriological and pathological studies of Bradford, Wilson, Bashford, and Holmes have furnished increasing evidence that a type of multiple neuritis exists which possesses all the features of a specific infectious disease. Although the organism has not been identified, the disease has been transmitted to the monkey, with the production of the symptoms and pathological lesions characteristic of the disorder in man. A living virus, obtained from cultures of the nervous tissue in fatal human cases, when injected into lower animals, is said to reproduce the disease and to be subsequently recovered from the fluid and tissues of the inoculated host.

Pathological examination of the nervous system, by Dr. Gordon Holmes, in 2 fatal cases of febrile polyneuritis revealed no evidence of active inflammation in the brain, cord, or meninges; but the anterior horn cells of the spinal cord and the cortical Betz cells were swollen, irregular, and in a process of disintegration. In the sciatic nerve a number of small fibres were undergoing degenerative changes. More recent studies have shown, however, that the lesion is not confined to the peripheral nerves and the lower motor neurone; but that, very often, the central nervous system and posterior root ganglia are severely affected. Foster Kennedy, in collaboration with Sir John R. Bradford, E. I. Bashford, and J. A. Wilson, has examined a number of pathological specimens from which he concludes that in some instances, at least, the polyneuritic features are associated with evidences of involvement of the spinal roots and central nervous tissue; and he has, accordingly, designated the disease as "infective neuronitis." Degenerative changes were also noted in the anterior and posterior cornua, and to a lesser degree in the cerebral cortex and pontile nuclei. The ganglion cells were surrounded by a moderate lymphocytic infiltration, and the peripheral nerves exhibited disseminated changes in the parenchyma; but the meninges showed no evidence of inflammation.

The symptoms of acute febrile neuritis may be initiated by a prodromal period in which evidences of the general infection predominate, or the neuritic symptoms may be the outstanding feature from the beginning. As a rule, the onset is sudden with a moderate rise in temperature, tachycardia, malaise, nausea, vomiting and, rarely, a chill. Pain in the legs and in the lower back is often persistent for a few days, when the paralytic symptoms appear and progress to their full development within a week or ten days from the onset. The legs are, as a rule, first involved and the proximal muscles are only slightly less affected than those at the periphery. The paralysis soon affects the arms, and facial diplegia is a characteristic feature. The other cranial nerves are rarely implicated, but weakness of the masseters and extraocular palsy have been noted; and difficulty in swallowing, a sense of constriction in the upper esophagus, and speech disorders are among the early symptoms. The muscles of the back, neck, and abdomen are sometimes involved, and Hayward has observed rigidity of the neck and Kernig's sign. The pupillary reactions are said to be unchanged.

In the beginning the deep reflexes may be increased, and numbness, tingling, and paresthesia are often experienced in the distal portion of the extremities. Hewson has found the diaphragm occasionally affected.

When the disease is fully developed, the legs are flabby and toneless, and the paralysis is symmetrical and wide-spread, although all of the muscles may not be equally affected. Usually, the legs suffer more severely than the upper extremities. Fibrillary tremor and contractures have not been noted. The tendon reflexes are generally abolished, but the cutaneous reflexes, with the exception of the plantar response, are often retained. Variable degrees of cutaneous sensory disorders have been observed. The postural sense and coördination are often defective, and hyperesthesia and muscle tenderness are sometimes present; but the sensory changes are not particularly prominent except in cases of well-marked neuritis. Trophic disorders are uncommon, and out-spoken sphincter paralysis is unusual. The urine is said to be free of sugar and albumin, and the spinal fluid is generally normal. In rare instances mild psychic disturbances have developed.

The course of the disease is acutely progressive, and usually reaches its maximum intensity within two or three weeks, when evidences of improvement make their appearance. Pulmonary complications may result in a fatal termination, and the mortality of the disease is estimated at about 26 per cent.

The sudden onset, the early improvement, the facial involvement, the loss of the tendon reflexes, the sensory changes, and the usual absence of sphincter disorders are of diagnostic importance. Nevertheless, it may be necessary to distinguish the disease from acute myelitis, poliomyelitis, Landry's paralysis, and the more common forms of toxic or infectious neuritis. The typical paraplegia, with its upper segmental level, the sphincter disorder, the pyramidal tract signs, and the absence of cranial nerve involvement are significant of myelitis; while the absence of sensory disorders together with the more rapid evolution and irregular distribution of the paralysis in poliomyelitis are valuable differentiating features. In Landry's paralysis the affection is rapidly ascending; the trunk and respiratory muscles are involved; and in most instances a fatal termination ensues, before the cranial nerves are implicated. Differentiation of the more common forms of multiple neuritis may be facilitated by determination of the etiological factor and the recognition of the general symptoms of metallic poisoning. Treatment is largely symptomatic and eliminative.

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